



Relapses of Differentiated Thyroid Cancer

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Thyroid cancer is the most common endocrine gland malignancy and accounts for 1-3% of the overall cancer incidence [1]. Despite its relatively modest place in the structure of malignant tumors, the problem of thyroid cancer has been seriously worrying scientists and doctors from various fields of medicine in recent decades. This is largely due to the extremely rapid increase in morbidity among young and middle-aged people, which is associated with an increase in radiation exposure. Despite the more than a century-long history of developing treatment tactics for thyroid cancer, a single treatment algorithm still does not exist. Even in such a large medical center, the range of operations performed is extremely wide, from enucleation of the tumor to extirpation of the thyroid gland and 2-way preventive cervical lymph dissection. To date, most clinicians agree on only one thing: the main method of treating primary tumors and regional metastases is surgical intervention, which often allows for a complete cure. At the same time, it should be noted that for most malignant tumors, the survival rate of patients is primarily taken into account, while for differentiated breast cancer, not only the life expectancy, but also the frequency of relapses and metastases of the tumor becomes important. Relapses may also occur at a later time after 10 or more years, and therefore long-term, lifelong monitoring of patients is necessary [12]. Treatment of patients with relapses and regional metastases is a complex task. Surgery still plays an important role in the treatment of this pathology. The choice of treatment tactics in patients with local recurrences of thyroid cancer should be differentiated, taking into account a number of factors. When evaluating indications for re-intervention, it is necessary to take into account the prognostic factors characteristic of breast cancer: gender, age, the volume of previous one-surgery, the histological structure of the tumor, as well as objective follow-up data. But the main factor is the assessment of the adequacy of the volume of resection of the affected organ during the first operation. Often, the cause of recurrence is partial resection or enucleation of the tumor node. Therefore, prevention of relapses can be an adequate volume and accurate execution of the first surgical intervention. During operation, observe the following points: be sure to conduct a thorough and wide audit of thyroid-lesions and areas of regional metastasis (paratracheal region, loaded in a space region of the vascular-nerve bundles); the secretion of the thyroid gland should be extracapsular, i.e., ligation of the upper and lower thyroid arteries and visual control of the recurrent nerves. To avoid injury to the recurrent nerve, do not apply clamps to the vessels of the gland; make a thorough assessment of the impact on the lymph nodes (the number, location and consistency of nodes, the condition of the capsule, etc.); to avoid implantation of metastases, the macroscopically damaged gland tissue should not be stitched or injured; in cases of doubtful malignancy, the final method of intraoperative diagnosis should be used, and an urgent biopsy should be performed. In recent years, breast cancer surgery has reached a high level of excellence. Nevertheless, to this day, many of its fundamental aspects are subject to further scientific study. The main issues discussed in differentiated forms of thyroid cancer are the choice of an adequate amount of thyroid surgery, as well as the indications and volume of surgical intervention in areas of regional lymph outflow. When determining the scope of thyroid surgery, there are 2 main opinions: the first is that regardless of the size of the tumor and other prognostic factors (morphological structure, age), thyroid extirpation is

necessary in all cases of cancer [7, 14]. Formulation of the principle of complete removal of the thyroid gland "principle" is supported by the following: reduction of the growth of thyroid cancer; reduction of the likelihood of local recurrence and IU of metastasis; reduction of the likelihood of repeated interventions, from which there is a high risk of complications; prevention of cancer in thyroid metastasis; prevention of the development of anaplastic cancer on the background of differentiated tumor; scintigraphy of the whole body with iodine-131 has a high diagnostic value compared with the intervention of the State in which the remains of thyroid tissue; determining the level of thyroglobulin has a high specificity for the diagnosis of recurrent disease and metastasis; treatment of recurrence or metastasis (distant especially governmental) more efficiently in the absence of residual TKA neither of the thyroid gland. Proponents of the organ-preserving method of surgical treatment of differentiated forms of thyroid cancer proceed from the point of view that in the absence of tumor growth beyond the lobe, hemithyroidectomy with an isthmus can be limited [1, 3, 4, 6].

This position is the authors prove the following circumstances: doubt high frequency of multicentric growth; the presence of multicentric microscopic foci of cancer growth does not mean they are implemented in the IP nodular tumor, the risk of developing anaplastic cancer on the background of high-grade tumors are exaggerated and not confirmed in clinical practice; the trauma of repeated operations not greater than that in resection of the thyroid gland; hormone replacement therapy after resection of the thyroid gland prominent never leads to normalization of the endocrine balance; figures 10-year survival of patients with differentiated forms of thyroid cancer is almost the same when you organization and "aggressive" approach. The discussion on the main controversial issues of surgical treatment of thyroid cancer continues. There are many publications on this topic, but no real serious international studies have been conducted. Analysis of the causes of regional metastases indicates that there is no consensus regarding surgical interventions on regional lymph collectors. At the same time, opinions differ both on the volume of cervical lymph dissection and on the expediency of preventive removal of regional lymph nodes. Proponents of such surgery assume that clinically undetectable micrometastases in lymph nodes can become a source of dissemination of the tumor process. To prove the correctness of such tactics of treating thyroid cancer, reference is made to the data of S. Noguchi et al. [15], who found micrometastases in non-palpable regional lymph nodes in 81.8% of cases. On the other hand, most clinicians [1, 3] claim that prophylactic removal of regional lymph collectors in patients with differentiated forms of thyroid cancer does not affect the outcome of the disease at all. By the way, when analyzing the clinical material, the same S. Noguchi et al. It was shown that in patients who did not undergo preventive removal of lymph nodes, regional relapse occurred only in 9.3% of cases. The authors explain the results of these studies by spontaneous regression of micrometastases after removal of the primary tumor. Although the question of the advantages of preventive lymphadenectomy over curative lymphadenectomy is still open, our own clinical experience confirms our opinion that it is inappropriate to remove non-palpable lymph nodes. We are deeply that attempts to find a more reliable method of detecting micrometastases in order to ensure that all lymphadenectomies are curative are justified. Recent publications have reported on the prophylactic removal of sentinel lymph node SLN (sentinel lymph node SLN). To visualize the "standing" lymph nodes, ultrasound examination, scintigraphy using a "radio probe" and special dyes are used directly at the time of intervention. An interesting technique was proposed by A. F. Romanchishin in patients with thyroid cancer [6]. For this purpose, 0.1-0.8 ml of 1% isosulfan blue alcoholic solutions of methylene blue and brilliant green were injected into the affected lobe, which stained the lymph nodes for 3-5 minutes. A small number of observations did not allow the author to make a final conclusion about the effectiveness of this diagnostic procedure. To date, there are many classifications of intervention on the lymphatic collectors of the neck. With regard to thyroid cancer, two modifications of the thyroid gland are most widely. 1) the so-called "thyroid" version of the operation Krail, developed by R. I. Wagner in 1962 [1] 2) [3]. The principal advantage of the first modification of lymphadenectomy is that a single block of removed tissues includes all groups of jugular lymph nodes and lymph nodes of the posterior junction, which are often affected by thyroid cancer. Providing for the obvious radicalism of the intervention, this technique has significant drawbacks in terms of cosmetic flaws (neck deformity, atrophy of the thyroid muscle) and the risk of blood circulation disorders in the elderly, etc. Recognizing the lower traumatic nature of fasciectomy of the cervical tissue, it is necessary to know that this operation is inferior to the "thyroid" version of the operation. The extreme is radical, since the preservation of the internal jugular vein and nodular muscle

creates a risk of lymphogenic and hematogenic spread of the tumor. The tendency to decrease the volume of removed tissues during lymphadenectomy can be justified only by analyzing prognostic factors, including the main ones are the prevalence of the process, the tumor's growth of the lymph node capsule, the ingrowth of the primary tumor and metastases into neighboring structures, the histological structure of the tumor, and age [2, 21, 22].

Over the past 10 to 15 years, our clinic has reviewed the position of fasciocellular removal of fiber, including lateral triangle lymph nodes and retrosternal lymph nodes. "Thyroid" version of the operation "Krailya" is performed only in the presence of a conglomerate of metastatic nodes, when the capsule of lymph nodes sprouts or grows into neighboring structures, with regional recurrences. At the same time, it should be borne in mind that often a surgeon operating on a patient with thyroid cancer is tempted to limit himself to a smaller intervention. There is a struggle for justice between thyroidectomy and the desire to maximize medical and social rehabilitation. The majority of Russian surgeons support organ-preserving surgeries for differentiated thyroid cancer. Perhaps this is due to the fact that in Russia there is only one center for the treatment of patients with radioactive iodine (Obninsk), and as you know, radioiodine therapy after extirpation of the thyroid gland actually reduces the risk of developing a relapse of the disease. Arguments of proponents of sparing operations and proponents of more aggressive methods over the past 15-20 years have not changed the essence of the contradictions regarding the scope of surgery for breast cancer. A number of surgeons with accumulated clinical experience have revised their position on this issue in the direction of expanding the indications for thyroid extirpation. The desire to limit indications for thyroid extirpation is dictated by the fear of possible complications (recurrent nerve paresis, parathyroid gland insufficiency). From an oncological point of view, thyroid extirpation followed by systemic radioiodine therapy is considered by most surgeons to be the method of choice for treating recurrent thyroid cancer. With appropriate experience and high surgical technique, total thyroidectomy can be performed with minimal risk of postoperative complications. The high technique of the operation, the use of parathyroid gland staining during the operation, as well as autotransplantation of parathyroid glands can dramatically reduce the risk of parathyroid insufficiency. In addition, the appearance of advanced hormonal drugs can significantly improve the quality of replacement therapy in the postoperative period. Many studies by foreign researchers [12, 14] have demonstrated a lower percentage of recurrences of differentiated thyroid cancer after total thyroidectomy and reported an increased survival rate in this group of patients compared to the group where a smaller operation was performed. In addition, differentiated thyroid cancer retains the ability to capture and utilize iodine, which makes it possible to use it for diagnosis and for therapeutic purposes.

In addition, cells of differentiated thyroid gland synthesize TG, the concentration of which in the blood after extirpation of the thyroid gland is a fairly sensitive marker of relapses and metastases [16]. Retrospective analysis of the factors predisposing to tumor recurrence in 585 patients with papillary microcarcinoma of the thyroid gland performed at the Mayo Clinic showed that the presence of metastases in the regional lymph nodes and organ-preserving operations on the thyroid gland obviously increase the risk of relapse of the disease [22]. According to the Gustav Clinic, according to a study conducted in Roussy (France), patients with papillary thyroid cancer are often multicentric, and therefore a complete thyroidectomy reduces the risk of tumor recurrence by 4 times compared to the removal of half of the organ [2]. At the same time, there are many cases when thyroid cancer is not diagnosed before surgery. The surgeon is obviously sure of the diagnosis of goiter or adenoma and performs a savings operation. Urgent histological examination is not always performed, and only after 1-2 weeks it turns out that the patient has a qualitative process. In such situations, it is necessary to determine treatment tactics in relation to patients who have not been operated radically, in the absence of visible signs of the disease. And the first question is whether to operate on the patient again, what is the optimal time for a second operation, and to what extent the intervention should be performed. In such a situation, it is equally difficult to decide on a second operation and refuse it. In such patients, the suggestion of a second operation, and even in a short time after the first intervention, causes severe psychological trauma. Literature data on this issue are contradictory. According to the data of the P. A. Herzen Moscow Institute of Cancer Research [1,3], if there are no clinical signs of breast cancer recurrence, a second operation should not be rushed at all, and monitoring is recommended in such cases. At the same time, we take into account the fact that only 61.6% of patients were diagnosed with cancer in the remaining thyroid tissue after repeated surgery. Repeated operations should have clear indications of a cytologically confirmed relapse. Examination of patients with suspected recurrence of thyroid cancer should,

if possible, begin with determining the scope of the first operation. Ultrasound, radionuclide scanning of the thyroid gland is used to solve this scanning problem. If it is not possible to review the micro-preparations of the removed tumor, then a puncture biopsy of the recurrent node is necessary. To assess the extent of recurrent tumor spread, computed tomography of the neck trachea and laryngoscopy are required to assess vocal folds due to recurrent nerve paresis.

Restriction of mobility or immobility of the holofold fold should be considered by the anesthesiologist during intubation and the surgeon, who should spare the remaining recurrent nerve to avoid acute respiratory disorders after surgery. If there are signs of involvement of the trachea and esophagus, tracheo- and esophagoscopy are indicated. These studies make it possible to verify the feasibility of surgical intervention, the possibility of which largely depends on the nature of involvement of the trachea, esophagus and large vessels in the tumor process. Proponents of the aggressive approach, primarily Americans [22], believe that the minimal intervention for recurrent thyroid cancer can be immediate extirpation of the thyroid gland with subsequent radioiodotherapy. On the one hand, repeated operations for thyroid cancer, as already noted, are always very painful for patients, and on the other hand, they are dangerous for the development of severe postoperative complications. Therefore, the operating surgeon should be aware of some special features of repeated surgery. First of all, it is necessary to remember about a good wide access, which involves cutting the skin to the lateral edges of the nodding muscles with mandatory dissection of the old postoperative scar. This makes it possible to conduct an audit of the remnants of the thyroid gland and areas of regional lymphatic outflow, including the paratracheal tissue and the anterior mediastinum. Often, scar tissue can resemble a tumor and thus make it difficult to navigate. In such cases, the approach to the thyroid gland or its bed is justified through unchanged muscles that need to be crossed above and below the scar tissue, and the fixed muscles are removed along with the recurrent tumor. It should be borne in mind that with relapses of differentiated thyroid cancer, the tumor can grow into the laryngeal wall, trachea, and esophagus. In such cases, it is advisable to start mobilizing the thyroid gland remnants from healthy tissues, isolate the unchanged part of the thyroid gland, mobilize it or cross it, go to the anterior surface of the affected organs and only then separate the tumor. If a tumor is suspected to be associated with the esophagus, a thick probe should be inserted into the esophagus immediately after intubation. At the same time, if the tumor grows to the wall of the esophagus, most often it is possible to limit the resection of the muscle layer without damaging the mucous membrane. Repeated operations for recurrent thyroid cancer dramatically increase the risk of damage to the return nerves and parathyroid glands. They can be soldered to the tumor node and do not differentiate well among the scars. If the tumor does not grow into the recurrent nerve, it can be isolated distal to the lower pole of the tumor node, take a rubber band, remove the empty holder and gradually release the entire length of the tumor. When the source of relapse is the upper pole of the thyroid gland, the tumor node can grow into the laryngeal cartilage. If a recurrent node is isolated, there is a risk of damage to the upper laryngeal nerve, which leads to epiglottis paresis. The act of swallowing is disrupted, and there is a risk of pneumonia. Serious difficulties are encountered in repeated operations for regional relapses. They are primarily associated with cicatricial fusion of metastatic nodes with large vessels. Most often, there is an intimate connection between the recurrent tumor and the wall of the internal jugular vein. Isolation of the trunk of the common carotid artery, as a rule, does not present great difficulties. During repeated operations, it is crucial to start isolating elements of the neurovascular bundle in unchanged tissues. First of all, make sure that the common carotid artery can be separated from the tumor. When planning operations for large recurrences of thyroid cancer, it is necessary to plan the possibility of vascular plastic surgery. To an even greater extent, it is necessary to provide for plastic surgery of the trachea when a recurrent node grows into it. Often, during extended operations for primary thyroid cancer, the surgeon meets with the growth of the primary tumor to the trachea and leaves tumor tissues on it. Naturally, these areas are the source of relapse that destroys the tracheal wall. In recent years, most surgeons are inclined to perform extensive operations with the removal of a recurrent tumor along with the removal of tissues surrounding the recurrent tumor, trachea, esophagus, larynx due to the lack of reliable radiation treatment, especially for papillary structure of the tumor. The justification of such operations is explained by the rather slow growth of a recurrent tumor, which for a long time has a "local" character and does not extend beyond the neck. According to E. A.'s data, according to V. V. Valdina [1], approximately one third of patients with papillary thyroid cancer die without distant metastases.

The greatest experience of such crippling and traumatic operations is accumulated by American and Japanese surgeons patients with papillary thyroid cancer, in whom the tumor sprouted in the trachea, reported success in treatment. Circular tracheal resection was performed with removal of 3 to 10 tracheal rings, followed by end-to-end anastomosis. Of these 24 patients, 17 people are alive for 3 to 8 years, including 13 - without signs of relapse. However, there is another point of view regarding the treatment tactics for locally advanced thyroid cancer and relapses [8, 24]. The authors recommend limited resections with the protection of important anatomical structures and often with the preservation of plates of tumor tissue, suggesting further radiation therapy (radioactive iodine or external radiation). G. Wolf et al. [24] believe that the combination of limited surgery with remote irradiation and brachytherapy and endoscopic laser therapy can achieve complete local regression of the tumor if thyroid cancer grows or relapses into the larynx and trachea. An example of successful palliative treatment of recurrent thyroid cancer using modern methods can be a therapeutic algorithm that combines argon plasma coagulation and photodynamic therapy. At the N. N. Petrov Research Institute of Oncology, we observed 3 patients with recurrent thyroid cancer growing into the trachea and large vessels of the upper thoracic aperture. Large degree of spread excluded the possibility of surgical intervention. Patients were admitted at various times after the first surgical intervention with the phenomenon of tracheal obturation in an extremely severe condition. Argon plasma recanalization was performed and the second stage was photodynamic therapy with the use of Photoditazine™ and laser device "Atkus". The patients easily underwent treatment. There was a slight swelling of the larynx and trachea, which did not require medication and resolved independently. All these patients show slow tumor growth, which requires repeated argon plasma coagulation and PDT sessions every 6 months. However, these patients are alive for more than 4 years with a very satisfactory quality of life. Many clinicians are of the opinion that the radical nature of surgical intervention in the recurrence of thyroid cancer is very conditional, and not so much in surgical terms, but in biological terms, due to the presence of subclinical metastases. Therefore, in order to increase the effectiveness of treatment of local and regional relapses of differentiated forms of thyroid cancer, combined approaches are justified, which involve combining surgery with radiation and, to a lesser extent, hormonal exposure. Despite serious theoretical and experimental justifications, the expansion of the range of adjuvant radiation effects in the treatment of breast cancer relapses in the form of widespread use of systemic radiation therapy (radioactive iodine) in our country is hindered by an extremely weak material and technical base.

Conclusions: relapses of differentiated thyroid cancer are a diverse and difficult pathology to treat. Our own clinical experience convinces us that the return of the disease in most cases is associated not with a true relapse of the disease, but with the defects of the first operation. Mistakes are made both for the primary tumor and regional metastases. This is primarily due to improper revision of the thyroid gland and areas of regional metastasis. Analysis of the causes of regional recurrences shows that partial, obviously non-radical lymphadenectomies are often performed. Usually, only enlarged, clearly metastasized lymph nodes are removed in violation of the zoning and case principles. Thus, the upper boundary of the removed block does not reach the level of bifurcation of the common carotid artery, as a result, the group of upper jugular lymph nodes, which are often affected by metastases, is not removed. On the other hand, the upper parathyroid lymph nodes, which often cause the development of regional relapses, are not removed. As already mentioned, implantation metastases are caused by technical errors during the first operation, which lead to a violation of the integrity of the tumor, its "crushing" and scattering of tumor material in the surgical area. This is sometimes caused by a small skin incision and a deep wound. Analysis of the literature data and our own experience shows that surgical interventions for relapses of differentiated thyroid cancer are prognostically favorable. According to the Petrov Research Institute of Oncology, among patients operated on for differentiated forms of thyroid cancer, the 5-year survival rate was 92%. Despite the traumatic nature, there is no doubt that it is advisable to perform extended operations when relapses grow into the trachea and larynx. Well-planned operations with this degree of process spread will allow you to expect a very satisfactory result. The use of modern methods of radiation therapy, physical and chemical techniques together with mountain monotherapy makes it possible to extend the life span of this category of severe patients while maintaining a good quality of life.

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