

MODERN THERAPY FOR NODULAR GOITER

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Abstract: Introduction: *To date, thyroid surgery has undergone major changes in terms of preoperative assessment of thyroid nodules. Various systems are used to evaluate thyroid nodes using ultrasound, one of which is the ACR TIRADS system, proposed by the American College of Radiology (American College of Radiology). A special system of cytological evaluation of these nodes according to the updated Bethesda classification adopted in 2017 is also used. This article presents data on the use of ACR TIRADS and Bethesda systems in patients who underwent surgery on the thyroid gland in the VITAMED clinic in Tashkent in the period from 01/08/2019 to 03/12/2020.*

Objective: *To show and evaluate the experience of using ACR TIRADS and Bethesda systems in the practice of thyroid surgery. To evaluate the correlation between the results of a preoperative assessment using these systems and the results of a histopathological study.*

Materials and methods: *1378 patients were examined. Of these, 158 patients were operated on in 2019 for nodular (n = 70) or mixed non-toxic (n = 31), diffuse toxic (n = 22), mixed toxic (n = 6), toxic nodular goiter (n = 15), as well as patients with autoimmune thyroiditis (AT) (n = 7) and patients with primary hyperparathyroidism simultaneously with the presence of thyroid nodules or with diffuse toxic goiter (n = 7). Ultrasound diagnostics using the ACR TIRADS system and a fine-needle aspiration biopsy (FNA) followed by a cytological evaluation using the Bethesda system were used for their preoperative evaluation. During the operation, express diagnostics of the removed nodes was performed. Subsequently, after the final histology, the data of cytology and express diagnostics and preoperative node evaluation were compared according to the results of ultrasound using the ACR TIRADS system.*

Results: *Data obtained from the use of ACR TIRADS and Bethesda systems have been shown to be effective in detecting thyroid cancer. 90.5% of the thyroid cancer revealed by the final histology, were rated before the operation by ACR TIRADS classification in categories TIRADS -3, TIRADS-4, TIRADS -5, in 19%, 34%, 37.5% of cases, respectively. According to the results of the FNA, 69% of thyroid cancer was preoperatively assigned to the three Bethesda classification categories, as B-IV - 41%, B-V - 22%, B-VI -6%, respectively. The indications for the operation were cases of confirmed thyroid cancer (n = 3), suspected thyroid cancer (n = 81), toxic goiter (n = 43), primary hyperparathyroidism and the simultaneous presence of thyroid nodes or diffuse toxic goiter (n = 7) and the presence of symptoms compression and / or substernal growth of thyroid nodes (n = 24). 101 total and near-total thyroidectomies, 15 subtotal thyroidectomies, 25 hemistromectomies, 17 extended or economical thyroid lobe resections were performed. During express histological diagnosis, all 100% of thyroid cancer cases were assigned to categories B-IV, B-V, B-VI in 28%, 58% and 16% of cases, respectively. According to the results of the final histology, 32 cases of thyroid cancer were identified (13 papillary*

carcinomas (41%), 8 (25%) follicular carcinomas, 10 (31%) follicular variant of papillary carcinomas, 1 (3%) undifferentiated carcinomas.

Conclusions: *The use of ACR TIRADS and Bethesda systems in the preoperative assessment of thyroid nodules is effective in detecting malignant tumors. The use of the Bethesda system for the cytological evaluation of smear materials on glass from thyroid nodules after their resection during surgery is effective in detecting thyroid cancer and adjusting the volume of surgical intervention.*

Introduction. The main task in the management of nodular goiter is to minimize the number of unnecessary operations and not to miss cases of thyroid carcinoma. The main indications for surgery in the presence of thyroid nodules are the following: the presence of thyroid cancer, the suspicion of thyroid cancer according to the results of FNA and ultrasound worrisome signs, the presence of symptoms of compression or substernal growth of the nodule, the presence of a voice change associated with the thyroid nodule(s), the presence of a toxic nodule(6). If there is a suspicion of the presence of a thyroid gland nodule or the presence of a palpable nodule, diffuse enlargement, an ultrasound diagnosis of the thyroid gland is necessary. When a nodule is identified using this method, the visualized nodule is evaluated according to a number of echo-graphic features (shape, echo structure, echogenicity, shape of the edges of the nodule, the presence of inclusions inside the nodule), and then summing up all these data, a conclusion is made regarding the degree of possible malignancy. At the moment, there are various systems for evaluating thyroid nodules and determining their possible malignancy (classification of malignancy of nodules according to ATA, K-TIRADS, EU-TIRADS, British U-grade). One of these classification systems is the TI-RADS system proposed in 2017 by the American College of Radiology (ACR TI-RADS) (8). There are 5 categories in this system, such as TIRADS - 1 (benign), TIRADS -2 (not suspicious), TIRADS -3 (mildly suspicious), TIRADS -4 (moderately suspicious), TIRADS - 5 (highly suspicious)

The use of this system gives clear indications for conducting a fine-needle aspiration biopsy or monitoring thyroid nodular formation, depending on the category of TIRADS and the size of the node.

Further, if there is evidence, biopsy material is taken from the thyroid gland with the above criteria and its cytological examination is carried out. According to the Bethesda system for reporting thyroid cytopathology, the following conclusions are possible (5):

Bethesda - 1 - Non-Diagnostic / Poor (N / N);

Bethesda - 2 - Benign (B);

Bethesda - 3 - Atypia of undetermined significance / Follicular lesion of undetermined significance (AUS / FLUS);

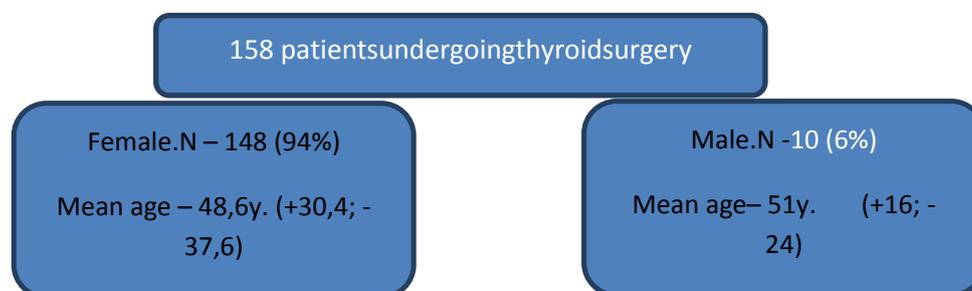
Bethesda - 4 - Follicular Neoplasm / Suspicion of Follicular Neoplasm (FN / SFN);

Bethesda - 5 - Suspiciousfor malignancy (SUS);

Bethesda - 6 - Malignant tumor (M).

Materials and methods.

158 patients were examined for nodular (n = 70) or mixed non-toxic (n = 31), diffuse toxic (n = 22), mixed toxic (n = 6), toxic nodular goiter (n = 15), and patients with autoimmune thyroiditis (AT) (n = 7) and patients with primary hyperparathyroidism simultaneously with the presence of thyroid nodules or with diffuse toxic goiter (n = 7). 101 total and near-total thyroidectomies, 15 subtotal thyroidectomies, 25 hemithyroidectomies, 17 extended or economical thyroid lobe resections were performed. Ultrasound diagnostics using the ACR TIRADS system and a fine-needle aspiration biopsy (TAB) followed by a cytological evaluation using the Bethesda system were used for their preoperative evaluation. Thyroid tissue was subjected to cytological evaluation during surgery - express histological diagnosis. Thus, a morphological assessment of the nodule was carried out three times - before the operation using a fine needle aspiration biopsy, during the operation - using an express histological examination, and finally, the final histopathological evaluation of the removed nodules. The volume of the operation depends on the first two stages of the morphological assessment. Mismatch of the results of rapid diagnosis and final histology can lead to repeated surgery of the patient. Therefore, the correct choice of surgical treatment tactics depends on the qualification of the pathomorphologist.



Results and discussion.

Table 1 below shows the obtained data on the assessment of nodes according to the ACR TIRADS system before surgery and on the results of a final histopathological examination of nodes after surgery in which thyroid cancer was detected.

Table 1. Thyroid nodules evaluated by the ACR TIRADS system and the results of a final histopathological examination of nodules with thyroid carcinoma.

	TR-1	TR-2	TR-3	TR-4	TR-5	N(%)
N (%)	3 (2%)	71 (45%)	49 (31%)	22(14%)	13(8%)	158(100%)
Thyroid carcinoma N (%)	0	3 (9,5%)	6 (19%)	11 (34%)	12 (37,5%)	32 (100%)
Risk of malignancy (%)	0	4%	12,5%	50%	92,3%	

Declared malignancy risks for categories (Tessler FN et al.)TR -1 / TR-2 - less than 2%, TR-3 - within 2-5%, TR-4 within 5-20%, TR-5 - more 20% (8). When comparing the data obtained, we can see that in the TR-2 category, the risk of malignancy in our study was 4%,

in TR-3 it was 12.5%, in TR-4 it was 50%, in TR-5 it was 92.3% . In almost all groups, the risk indicators of malignancy are higher than the initially declared figures by the American Association of Radiologists. In a study by A.A. Kvasova (1), it was found that the cytological result of B-VI (malignant) was found in 1.17%, 9.3% and 12.3% of the nodules, which were rated as TR-2, TR -3 and TR -4, respectively.

The numbers of cases are lower in our study. Most likely this is due to the fact that in the study, A. Kvasova calculations were carried out on a much larger number of nodules (3758 nodes). In another retrospective study, Timofeeva L.A. already analyzed 296 nodules with thyroid carcinoma, which were also divided into TIRADS categories (2). In categories TR-3, TR-4, and TR-5, thyroid carcinoma occurred in 4.7%, 41%, and 54% of cases. In our study, 32 (100%) cases of thyroid carcinoma were divided into categories TR-3, TR-4, TR-5 in 19%, 34% and 37.5% of cases, respectively. Again, comparing these data is very difficult, since the number of cases with thyroid carcinoma in the study of L. Timofeeva exceeded more than 9 times those in our study, and also in our study did not meet such a type of thyroid carcinoma as medullary carcinoma. When comparing the number of detected cases of thyroid cancer in our study, in the categories TR-4 and TR-5, it is seen that almost the same number of cases of thyroid cancer was found. In the TR-4 category, 11 cases were revealed, and in the TR-5 category, 12 cases were revealed.

This result may indicate the legitimacy of dividing the T4 category into subcategories T4a, T4b, and T4c, as proposed in the Kwak JY modification (7). A similar TIRADS system with subcategories was used in the study by Antonio R.J. (3), and 976 thyroid nodules were analyzed, of which thyroid carcinomas were detected in 123 nodes. These cases were divided into TIRADS classification categories and as a result, it was shown that carcinomas were found in categories TR-2, TR-3, TR-4a, TR-4b, TR-4c, TR-5 in 0.8%, 1, 7%, 16%, 43% 72%, and 91% of cases, respectively. At the same time, it was shown that out of the total number of nodules, 125 were rated as TR-2. During a cytological examination of the nodules of this category, carcinoma was detected in 1 case. In our study, from 71 TR -2 nodules in 3 of them, carcinoma was detected. These data suggest that in each case it is necessary to proceed from their clinical manifestations of the disease and make decisions individually.

Table 2 shows data on the results of FNA of thyroid nodules and the results of histopathological examination of nodules with thyroid carcinoma.

Table 2. The results of FNA of thyroid nodules and final histopathological examination of nodules with thyroid carcinoma.

	B - I	B – II	B – III	B – IV	B – V	B-VI	N(%)
N (%)	1 (0,5%)	112 (71%)	0	34 (21,5%)	8 (5%)	3 (2%)	158 (100%)
Thyroid carcinoma N (%)	0	10 (31%)	0	13 (41%)	7 (22%)	2 (6%)	32 (100%)
Risk of malignancy (%)	0	9%	0	38%	88%	67%	

The risk of malignancy for categories BI, B-II, B-III, B-IV, B-V, B-VI are 1-4%, 0-3%, 5-15%, 15-30%, 60-75% and 97-99%, respectively (2). When conducting FNA of thyroid nodules in our study, the following malignancy risk indicators were identified: B-I - 0%, B-II

- 9%, B-III -0%, B-IV - 38%, B-V -88%, B- VI - 67%. Categories B – I and B – III were not found in our study, possibly due to the relatively small number of samples. In category B-VI, the risk of malignancy was lower than stated in the Bethesda 2017 classification protocol (2). This is explained by the fact that in one case the FNA result of one of the nodule was evaluated as B – VI, and during express histological examination of this nodule was rated by the Bethesda classification as B – II. A hemithyroidectomy was performed. Subsequently, according to the results of the final histology, thyroid cancer was not detected.

Table 3 shows the results of express histological examination and the results of a histopathological examination of nodes with thyroid carcinoma.

Table 3.Results of express histological diagnosis of thyroid nodes and histopathological examination of nodes with thyroid carcinoma.

	B – I	B – II	B - III	B - IV	B - V	B-VI	N(%)
N(%)	0	116 (73,5%)	0	19 (12%)	18 (11,5%)	5 (3%)	158 (100%)
Thyroid carcinoma - N(%)	0	0	0	9 (28%)	18 (56%)	5 (16%)	32 (100%)
Risk of malignancy %	0	0	0	47%	100%	100%	

The results of express histological diagnosis of thyroid nodules gave the following malignancy risk figures: B-II - 0%, B-III -0%, B-IV - 47%, B-V -100%, B-VI - 100%. Category B-1 is not indicated here, since the finished resected node in the hands of a pathomorphologist cannot give non-diagnostic or unsatisfactory results when preparing a smear on glass.

Of the total number of nodules (n = 158), in the nodules evaluated as B – II (n = 116), in no case was thyroid cancer detected according to the results of a histopathological study. If we look at the results of category B-II in terms of FNA, we can see that in this category thyroid carcinoma was found in only 10 nodules out of 112 nodes and hence, a 9% risk of malignancy. And in category B - II, according to the results of an express histological examination, thyroid carcinoma was not detected in any of all 116 nodules according to the results of the final histopathological examination and hence the zero percentage of malignancy. Thus, category B - II obtained during express histological diagnosis after nodule resection is most reliable than category B - II obtained with FNA results before surgery.

Categories B-V and B-VI showed a 100% risk of malignancy according to the results of the final histological study in our study. So, after resection of the thyroid nodules, in 18 cases the nodules were rated as category B-V and in 5 cases, rated as category B-VI. With a final histopathological examination of all these nodules, thyroid carcinoma was detected in all cases. Ultimately, the meaning of an express histological examination of resected thyroid nodules during surgery is to adjust the volume of surgical intervention on the thyroid gland. In this case, it is clearly seen how the results of the FNA can differ from the results of an express histological examination of the resected thyroid nodules during surgery. Therefore, the significance of the latter is important in the practice of a thyroid surgeon.

If you look at category B-IV, we see that of the total number of nodes ($n = 158$), 19 (12%) of them were rated as B-IV. Subsequently, with a final histopathological examination of these nodes, thyroid carcinoma was revealed in 9 cases. Thus, the risk of malignancy was 47% in this category. All patients underwent total thyroidectomy. In all other benign cases, according to the results of the final histopathological examination, it would seem that total thyroidectomy can be considered as an unreasonably excessive intervention. However, if total thyroidectomy was not performed, then repeated surgery would have to be performed to remove residual thyroid tissue in 47% of patients, according to our study. For a more differentiated approach, in terms of treatment tactics for patients with category B-IV, it is necessary to accumulate experience in using molecular genetic panels to identify genetic mutations in this category. In a Beatriz G.C. study (4), 615 nodes were examined, of which 137 were evaluated as B-IV as a result of cytological examination and 49 (36%) of them had thyroid carcinoma. All patients underwent total thyroidectomy.

Conclusion.

The use of TIRADS and Bethesda systems in the preoperative assessment of thyroid nodules helps to choose the right tactics for patient management, namely to observe, operate and, if operated, to select the scope of the operation. The use of the Bethesda system for cytological evaluation of thyroid nodules before surgery and after their resection during express histological diagnosis is effective in detecting thyroid cancer and adjusting the volume of surgical intervention. The treatment of category B-IV nodes requires further research to select a more differentiated approach to treatment.

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