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INTEGRATED PREOPERATIVE STRATIFICATION OF DIFFERENTIATED THYROID CANCER BASED ON CLINICAL, ULTRASONOGRAPHIC, MORPHOLOGICAL, AND BIOMARKER PROFILES

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КОМПЛЕКСНАЯ ПРЕДОПЕРАЦИОННАЯ СТРАТИФИКАЦИЯ ДИФФЕРЕНЦИРОВАННОГО РАКА ЩИТОВИДНОЙ ЖЕЛЕЗЫ НА ОСНОВЕ КЛИНИЧЕСКИХ, УЛЬТРАЗВУКОВЫХ, МОРФОЛОГИЧЕСКИХ И БИОМАРКЕРНЫХ ПРОФИЛЕЙ

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KLINIK, ULTRATOVUSH, MORFOLOGIK VA BIOMARKER PROFILLARIGA ASOSLANGAN DIFFERENTSIATSIYALANGAN QALQONSIMON BEZ SARATONINING OPERATSIYADAN OLDINGI KOMPLEKS STRATIFIKATSIYASI.

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Цель: *оценка ценности клинических, ультразвуковых, цитологических, гистопатологических и биохимических характеристик дифференцированного рака щитовидной железы для предоперационной стратификации риска.* ***Материал и методы:*** *в дпроспективное аналитическое исследование были включены 202 пациента с гистологически подтвержденным дифференцированным раком щитовидной железы. В зависимости от окончательной гистологии пациенты были разделены на три: с папиллярной карциномой – 112, с фолликулярной карциномой – 63, с фолликулярным вариантом папиллярной карциномы – 27. Контрольная группа – 30 здоровых лиц. Все пациенты прошли комплексное клиническое обследование и высокоразрешающее ультразвуковое исследование щитовидной железы с оценкой эхогенности, краев, кальцификаций, васкуляризации и шейных лимфатических узлов.* ***Результаты****: установлено, что фолликулярный вариант папиллярной карциномы характеризуется более агрессивным течением и повышенными уровнями тиреоглобулина, антител к тиреоглобулину и ракового эмбрионального антигена. Интеграция TI-RADS, системы Bethesda и сывороточных маркёров улучшает предоперационную стратификацию риска.* ***Выводы:*** *комплексный мультимодальный подход, сочетающий клиническую оценку, стратификацию риска на основе ультразвукового исследования, цитологическую оценку, гистопатологию и биохимические маркеры, позволяет улучшить выявление агрессивных дифференцированных вариантов рака щитовидной железы до операции и способствует индивидуальному ведению пациентов.*

Ключевые слова: *дифференцированный рак щитовидной железы, TI-RADS, система Bethesda, тиреоглобулин, антитела к тиреоглобулину, раковый эмбриональный антиген, стратификация риска.*

Maqsad: *operatsiyadan oldingi xavf stratifikatsiyasi uchun differentsiatsiyalangan qalqonsimon bez saratonining klinik, ultratovush, sitologik, gistopatologik va biokimyoviy xususiyatlarining qiymatini baholash.* ***Material va usullar:*** *ushbu istiqbolli analitik tadqiqotga gistologik jihatdan tasdiqlangan differentsiatsiyalangan qalqonsimon bez saratoniga chalingan jami 202 bemor kiritildi. Yakuniy gistologiyaga qarab, bemorlar uch guruhga bo'lindi: 112 ta papiller karsinoma, 63 ta follikulyar karsinoma va 27 ta papiller karsinomaning follikulyar varianti bilan. Nazorat guruhi 30 ta sog'lom odamdan iborat edi. Barcha bemorlar qalqonsimon bezning keng qamrovli klinik tekshiruvidan va yuqori aniqlikdagi ultratovush tekshiruvidan o'tkazildi, ularda ekojenlik, chegaralar, kalsifikatsiya, qon tomirlanish va bo'yin limfa tugunlari baholandi.* ***Natijalar:*** *follikulyar papiller karsinoma yanada agressiv kechishi va tiroglobulin, antitiroglobulin antitelolari va karsinoembrion antigenining yuqori darajasi bilan tavsiflanganligi aniqlandi. TI-RADS, Bethesda tizimi va zardob markerlarining integratsiyasi operatsiyadan oldingi xavf stratifikatsiyasini yaxshilaydi.* ***Xulosa:*** *klinik baholash, ultratovushga asoslangan xavf stratifikatsiyasi, sitologik baholash, gistopatologiya va biokimyoviy markerlarni birlashtirgan kompleks multimodal yondashuv agressiv differentsiatsiyalangan qalqonsimon bez saratoni variantlarini operatsiyadan oldin aniqlashni yaxshilaydi va bemorlarni individual davolashni osonlashtiradi.*

Kalit so'zlar: *differentsiatsiyalangan qalqonsimon bez saratoni, TI-RADS, Bethesda tizimi, tiroglobulin, antitiroglobulin antitelolari, karsinoembrion antigeni, xavf stratifikatsiyasi.*

Differentiated thyroid cancer represents the most common endocrine malignancy worldwide. Although long-term survival is generally favorable, substantial heterogeneity exists with regard to tumor aggressiveness, patterns of invasion, and metastatic potential [1,6]. Papillary and follicular carcinomas, while grouped under the umbrella of differentiated tumors, exhibit distinct biological behavior and clinical outcomes.

Preoperative risk stratification remains a critical challenge, particularly in follicular-patterned lesions. Ultrasound-based classification systems such as TI-RADS and cytological assessment using the Bethesda system have improved diagnostic consistency, yet their predictive value varies across histological subtypes [2,3]. Biochemical markers, including thyroglobulin and anti-thyroglobulin antibodies, are routinely used in postoperative follow-up, while their preoperative significance remains incompletely defined [4].

Purpose of the study

To evaluate clinical, ultrasound, cytological, histopathological and biochemical characteristics of differentiated thyroid cancer depending on the histological subtype, as well as their overall value for preoperative risk stratification.

Material and methods

This prospective analytical study included 202 patients with histologically confirmed differentiated thyroid cancer who underwent evaluation and surgical treatment. Patients were divided into three groups according to final histology: papillary carcinoma (n=112), follicular carcinoma (n=63), and follicular variant of papillary carcinoma (n=27). A control group consisted of 30 healthy individuals.

All patients underwent comprehensive clinical assessment and high-resolution ultrasound of the thyroid gland with evaluation of echogenicity, margins, calcifica-

tions, vascularity, and cervical lymph nodes. Ultrasound findings were classified using the TI-RADS system [5]. Fine-needle aspiration biopsy was performed under ultrasound guidance and interpreted according to the Bethesda classification.

Preoperative serum levels of thyroglobulin, anti-thyroglobulin antibodies, and carcinoembryonic antigen were measured using standardized immunoassays. Histopathological evaluation included assessment of tumor size, T and N categories, capsular and vascular invasion, multifocality, and extrathyroidal extension [7].

Statistical analysis was performed using descriptive and inferential methods. Categorical variables were compared using the chi-square test, while quantitative variables were analyzed using non-parametric tests. Statistical significance was defined as $p<0.05$.

Results

The study included 202 patients with histologically verified differentiated thyroid cancer. A pronounced predominance of female patients (87.2%) was observed. Comparative analysis revealed significant intergroup differences in clinical presentation, ultrasonographic risk stratification, histopathological characteristics, and preoperative biomarker profiles.

Table 1 presents the clinical and demographic characteristics of the study population stratified according to histological subtype. Patients with the follicular variant of papillary carcinoma were significantly younger at diagnosis, while the sex distribution remained comparable across groups.

Table 1

Clinical and demographic characteristics of the study groups

Parameter	Papillary carcinoma	Follicular carcinoma	Follicular variant of papillary carcinoma
Female, %	90.2	82.5	81.4
Mean age, years	42.6±10.3	39.1±9.3	32.0±11.7

Ultrasound-based risk stratification demonstrated marked heterogeneity between histological variants. As shown in Table 2, high-risk TI-RADS categories were most frequently observed in the follicular variant of papillary carcinoma.

Table 2

Distribution of TI-RADS categories according to histological subtype

Group	TI-RADS 3	TI-RADS 4A	TI-RADS 4B	TI-RADS 5
Papillary carcinoma	10	18	32	52
Follicular carcinoma	12	21	18	12
Follicular variant	2	5	6	14

Histopathological examination revealed substantial differences in invasive characteristics. Table 3 summarizes the prevalence of adverse morphological features across study groups.

Table 3

Histopathological indicators of tumor aggressiveness

Feature	Papillary carcinoma, %	Follicular carcinoma, %	Follicular variant, %
Vascular invasion	8.9	41.3	55.6
Capsular invasion	19.6	49.2	51.9
Lymph node metastasis	48.2	22.2	59.3

Preoperative biochemical marker analysis demonstrated progressive elevation of thyroglobulin, anti-thyroglobulin antibodies, and carcinoembryonic antigen from papillary and follicular carcinoma to the follicular variant of papillary carcinoma (Table 4).

Table 4

Preoperative serum biomarker levels

Marker	Papillary carcinoma	Follicular carcinoma	Follicular variant
Thyroglobulin, ng/ml	34.8	28.6	62.4
Anti-thyroglobulin antibodies, IU/ml	63.4	41.2	78.5
Carcinoembryonic antigen, ng/ml	10.2	11.3	18.4

Discussion

This study demonstrates that differentiated thyroid cancer comprises biologically distinct entities that can be partially differentiated prior to surgery using integrated clinical, imaging, cytological, and biochemical assessment. The follicular variant of papillary carcinoma emerged as a subgroup with a distinctly aggressive profile.

Patients with this variant were diagnosed at a younger age and more frequently presented with compressive symptoms, suggesting rapid tumor growth and early local invasion. Ultrasonographic stratification revealed a predominance of high-risk TI-RADS categories, indicating that imaging features reflect underlying tumor biology.

Cytological findings emphasized persistent limitations of fine-needle aspiration biopsy in follicular-patterned lesions, reinforcing the need for adjunctive preoperative markers. Histopathological evaluation confirmed higher rates of vascular and capsular invasion and lymph node metastasis, supporting consideration of more extensive initial surgical management [8].

Elevated preoperative levels of thyroglobulin, anti-thyroglobulin antibodies, and carcinoembryonic antigen were associated with aggressive morphological features [9]. Although traditionally reserved for postoperative follow-up, these markers may provide additional value in preoperative risk stratification when interpreted in conjunction with imaging and cytology.

Several limitations should be acknowledged, including the single-center design and the absence of molecular profiling [10]. Future multicenter studies incorporating genetic and molecular data are warranted. Overall, integrated preoperative assessment may facilitate personalized surgical and postoperative strategies, potentially improving outcomes in patients with high-risk differentiated thyroid cancer.

Conclusions

1. An integrated multimodal approach combining clinical evaluation, ultrasound-based risk stratification, cytological assessment, histopathology, and biochemical markers enables improved identification of aggressive differentiated thyroid cancer variants prior to surgery and supports individualized patient management.

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Objective: *To evaluate the value of clinical, ultrasound, cytological, histopathological, and biochemical characteristics of differentiated thyroid cancer for preoperative risk stratification.* ***Material and methods:*** *A total of 202 patients with histologically confirmed differentiated thyroid cancer were included in this prospective analytical study. Depending on the final histology, the patients were divided into three groups: 112 with papillary carcinoma, 63 with follicular carcinoma, and 27 with the follicular variant of papillary carcinoma. The control group consisted of 30 healthy individuals. All patients underwent a comprehensive clinical examination and high-resolution ultrasound examination of the thyroid gland with assessment of echogenicity, margins, calcifications, vascularization, and cervical lymph nodes.* ***Results:*** *Follicular papillary carcinoma was found to be characterized by a more aggressive course and elevated levels of thyroglobulin, antithyroglobulin antibodies, and carcinoembryonic antigen. Integration of TI-RADS, the Bethesda system, and serum markers improves preoperative risk stratification.* ***Conclusions:*** *A comprehensive multimodal approach combining clinical assessment, ultrasound-based risk stratification, cytological assessment, histopathology, and biochemical markers improves the preoperative detection of aggressive differentiated thyroid cancer variants and facilitates individualized patient management.*

Key words: *differentiated thyroid cancer, TI-RADS, Bethesda system, thyroglobulin, antithyroglobulin antibodies, carcinoembryonic antigen, risk stratification.*

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