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ВИКОРИСТАННЯ ШКАЛИ TIRADS В ПРОҐНОЗУВАННІ РАКУ В ХВОРИХ З КІСТОЗНИМИ ВУЗЛАМИ ЩИТОПОДІБНОЇ ЗАЛОЗИ

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Реферат

Мета. *Провести аналіз ефективності застосування шкали TIRADS в модифікації Russ для прогнозування раку щитоподібної залози та порівняння діагностичних можливостей шкали у пацієнтів з тканинними та кістозними вузлами щитоподібної залози.*

Матеріал і методи. *Проведено ретроспективний аналіз карт стаціонарного хворого, оперованих протягом 2015-2016 років у клініці хірургії №1 Львівського національного медичного університету з приводу вузлових утворень щитоподібної залози. Стратифікацію ризику раку щитоподібної залози виконували оцінюючи заключення ультрасонографії згідно вимог шкали TIRADS за Russ. Отримані дані аналізували як для тканинних, так і для кістозних вузлів.*

Результати й обговорення. *Загалом з вузловими утвореннями щитоподібної залози було прооперовано 1033 пацієнти віком від 17 до 82 років. У 385 (37,3%) пацієнтів не вдалось провести стратифікацію TIRADS через брак інформації в описі протоколу ультрасонографії. В подальшому аналізі було розглянуто решту 648 випадків, серед яких доведено 96 (14,8%) випадків раку. Пацієнти були поділені на 2 групи: група I - "кістозні вузли" - 164 (25,3%) пацієнти; група II - "солідні вузли" - 484 (74,7%) пацієнти. У групі I відсоток раку щитоподібної залози склав 3,7%, а в групі II - 18,6% ($\chi^{2=}$21,655; p<0,00001). Відмічено також різницю в частоті "папілярної мікрокарциноми" серед кістозних та солідних вузлів, відповідно 1,2% та 3,5%. При використанні шкали TIRADS у прогнозуванні раку у хворих з кістозними вузлами щитоподібної залози виявлено її високу специфічність - 93,0%, тоді як чутливість шкали була низькою - 16,7%. При оцінці кістозних вузлів шкала TIRADS показала високу загальну діагностичну точність - 90,2%, проте в практичному її застосуванні виявлено низький рівень позитивного прогнозування раку щитоподібної залози (8,3%), особливо у порівнянні із тканинними вузлами (44,1%).*

Висновки. *Застосування ультрасонографічних шкал TIRADS є ефективним методом прогнозування раку щитоподібної залози. Частка раку серед кістозно-змінених вузлів щитоподібної залози суттєво нижча. Через низьку чутливість прогнозування раку шкали TIRADS в пацієнтів з кістозно-зміненими вузлами щитоподібної залози, випадки, які належать до TIRADS 2-4a, потребують ретельного спостереження.*

Ключові слова: *кістозні вузли щитоподібної залози, рак щитоподібної залози, TIRADS*

Abstract

TIRADS EFFECTIVENESS IN CANCER RISK PROGNOSIS AMONG PATIENTS WITH CYSTIC AND SOLID THYROID NODULES

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Aim. *To analyse the effectiveness of TIRADS scale modified by Russ for prediction of thyroid cancer and comparison of diagnostic capabilities of the scale in patients with solid and cystic thyroid nodules.*

Material and Methods. *Patients, who underwent surgery for thyroid nodules in period of 2015-2016 at the Department of Surgery No. 1 of the Lviv National Medical University were taken to research, and retrospective analysis was carried out. Stratification of thyroid cancer risk was performed by evaluation of ultrasonography findings according to the TIRADS scale. The obtained data were analysed for both solid and cystic thyroid nodules separately.*

Results and Discussion. *In total, 1033 patients aged 17 to 82 years were operated for thyroid nodules. In 385 (37.3%) cases we failed to stratify by TIRADS due to lack of information in ultrasonographic description. Subsequent analysis was done over remaining 648 patients, among which 96 (14.8%) cases of cancer were proven. Patients were divided into 2 groups: Group I - "cystic nodules" - 164 (25.3%) patients; Group II - "solid nodules" - 484 (74.7%) patients. In group I thyroid cancer prevalence was 3.7%, while in group II it was 18.6%. The difference in thyroid cancer incidence had a significant statistical probability (χ^2=21.655; p <0.00001). There was a difference in the frequency of "papillary microcarcinoma" among cystic and solid nodules: 1.2% and 3.5% respectively. In the prediction of cancer in patients with cystic thyroid nodules, TIRADS scale demonstrated a high specificity of 93.0%, while the sensitivity was low - 16.7%. The TIRADS scale in assessing of cystic thyroid nodules showed a high overall diagnostic accuracy of 90.2%, but the level of positive predictive value for thyroid cancer among cystic nodules was low - 8.3%, especially when compared to solid nodules - 44.1%.*

Conclusions. *TIRADS is an effective method in predicting thyroid cancer, especially among solid nodules. Cancer prevalence among cystic thyroid nodules is significantly lower compared to solid nodules: 3.7% vs. 18.6%. The low sensitivity of the TIRADS scale in patients with cystic thyroid nodules is 16.7%, and therefore cases with cystic nodules graded TIRADS 2-4a require precise follow up.*
Key words: *cystic thyroid nodes, thyroid cancer, TIRADS*

Introduction

The prevalence of nodular goiter is quite high and demonstrates a level of 15-24% in adult population worldwide [13], and 33% in endemic regions [8]. In 2014, the incidence of nodular goiter in Ukraine was 636 per 100,000 of population, and it continues to grow in recent years. Cystic thyroid nodule (CTN) - a mass with fluid component equivalent to more than 10% of volume [7] comprise 15-35% of all thyroid nodules [3, 10].

Among patients with thyroid nodules (TN) who undergo surgery, cancer is ultimately diagnosed in 5-35% of cases [4]. The incidence of thyroid cancer in Ukraine has also increased to 6.8 per 100,000 (almost 3,000 new cases yearly). There are no reliable signs or predictors of thyroid cancer, although there is a stereotype that cystic changes in TN testify in favour of their benign nature, as the prevalence of thyroid cancer among the CTN amounts only to 5.2-17.6% [6].

The goal in management of patients with TN is thyroid cancer risk assessment. Presently, the key role in differential diagnostics of TN is played by ultrasonography (USG) and, according to indications, fine-needle aspiration biopsy (FNA), but overall accuracy of USG in thyroid cancer detection is only 64-81% [2, 11].

Usually USG conclusion is descriptive, rarely contains quantitative indexes and is "operator-dependent" with significant subjectivity. To overcome the above restrictions, the USG can be implemented through the introduction of various diagnostic scales: TIRADS, U classification, ATA recommendation, ACR TIRADS, etc. [12], which makes it possible to convert USG into a more objective method and to avoid uncertain interpretations of clinical cases [9]. The TIRADS scale was proposed in 2009 [2] and initially facilitated the patients` selection for FNA, but afterwards was used mainly for prediction of thyroid cancer. In general, several modifications of the TIRADS scale were proposed, and the most recent, according to literary sources, is the TIRADS modification by Russ, published in 2011 by French researchers [9].

The purpose of our work was to determine the effectiveness of TIRADS by Russ modification in predicting thyroid cancer, and to compare the diagnostic capabilities of the scale between solid and cystic thyroid nodules.

Material and Methods

A retrospective analysis of 1033 hospital patients` cards was performed. All the patients underwent operation due to TN over two (2015-2016) years at Department of Surgery No. 1 of the Lviv National Medical University.

Besides general data (patient`s age and gender, thyroid nodules history), the thyroid status was also studied - TSH level, thyroglobulin, antibodies against thyroglobulin and the microsomal antigen. The USG determined the number of TN, the size of the dominant (the largest or suspected for malignancy) nodule, presence of liquid inclusions, etc. The results of FNA with cytological conclusion, type of surgical intervention, intraoperative (frozen section) and final histological examination were analysed.

According to the TIRADS scale, USG data were evaluated for the presence of cancer risk factors: the hypoechogenicity, nodule margins, presence of calcifications, extrathyroidal invasion, enlarged neck lymph nodules, etc. A certain combination of factors corresponded to the degree of cancer risk: 1, 2, 3, 4a, 4b, and 5. The received data were analyzed for both solid and cystic thyroid nodules and compared effectiveness - sensitivity, specificity, positive and negative predictive value, general diagnostic accuracy in predicting of thyroid cancer- was compared.

Obtained results were calculated using SPSS 11.5 for Windows statistical software. To

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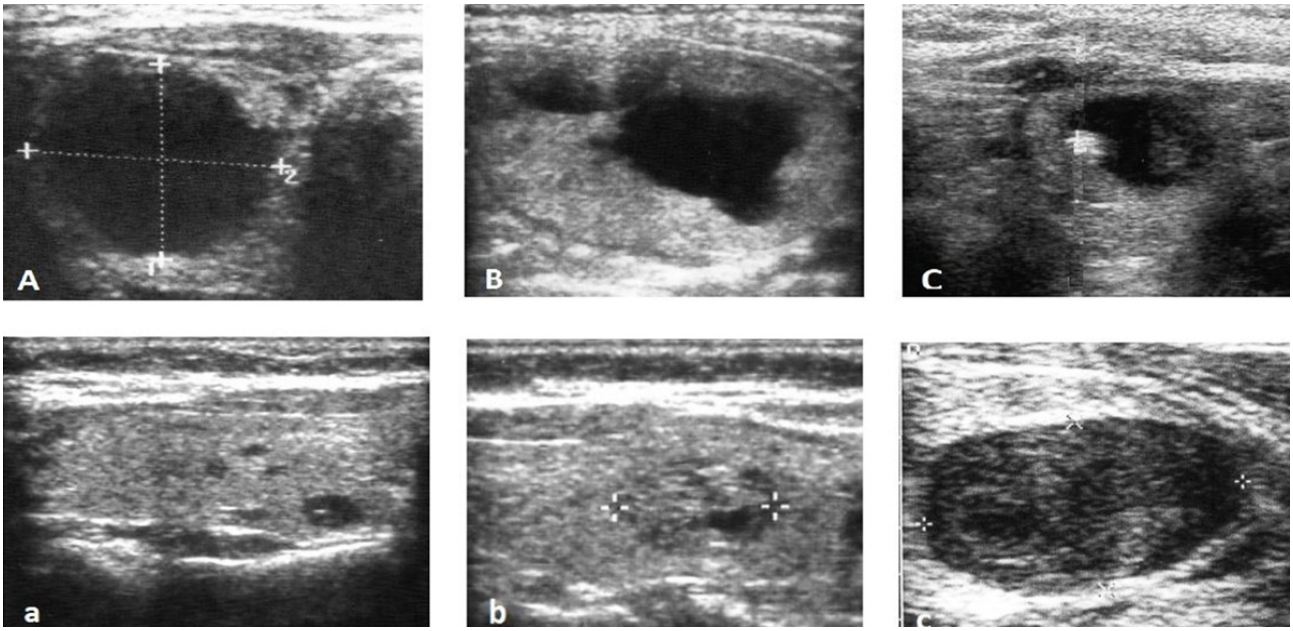

Figure 1
Cystic thyroid nodules: A Thyroid cyst - TIRADS 2; B - partially cystic isoechoic nodule - TIRADS 3;
C - microcalcification in cystic degenerated nodule - TIRADS 4a.
Solid thyroid nodules: a - "Spongiform" thyroid nodule - TIRADS 2;
b - isoechoic nodule with regular margin - TIRADS 3;
c - hypoechoic solid nodule - TIRADS 4a.

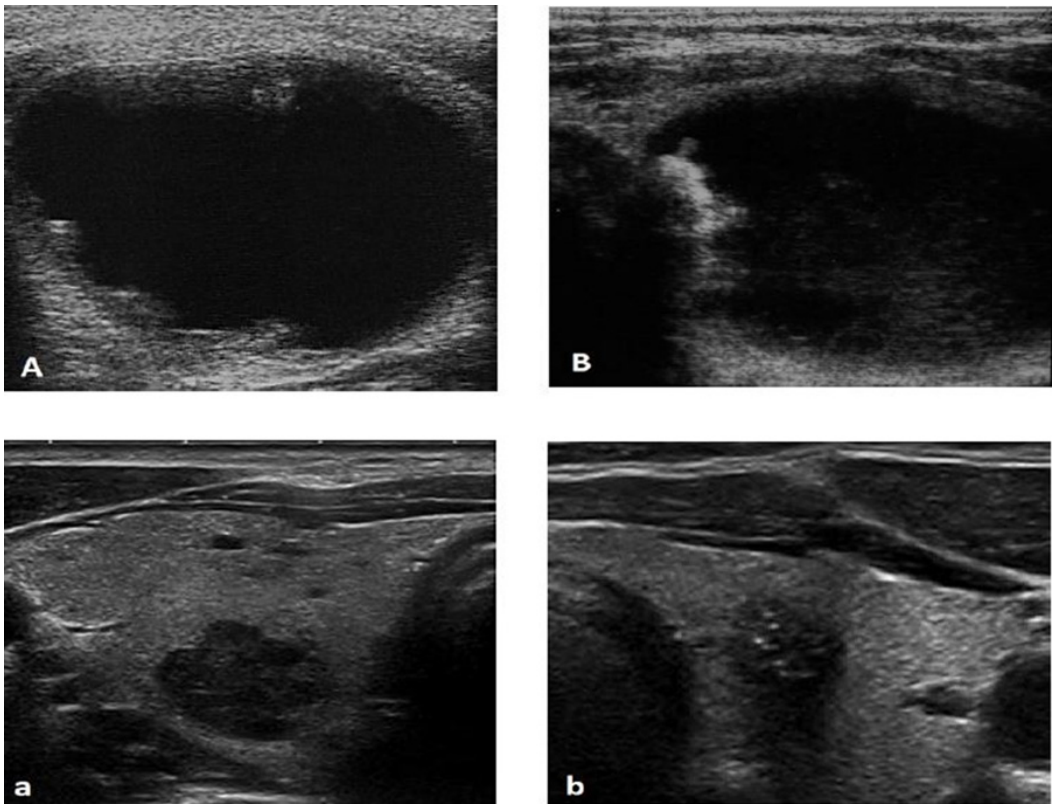

Figure 2
Cystic thyroid nodules: A - Predominantly cystic nodule with irregular margin inside cavity - TIRADS 4b;
B - predominantly cystic nodule with microcalcifications - TIRADS 4b.
Solid thyroid nodules: a - Markedly hypoechoic solid nodule with pseudolobular margin - TIRADS 4b;
b - hypoechoic solid nodule with irregular margin and microcalcifications - TIRADS 5

Table 1

Thyroid cancer risk stratification by TIRADS scale among CTN (n=164)

TIRADS (grade) Diagnosis	2 (n=9)	3 (n=102)	4a (n=41)	4b (n=12)	5 (n=0)
Colloid goiter (n=114)	7 (-)	70 (68.6%)	29 (70.7%)	8 (-)	-
Adenoma (n=39)	2 (-)	24 (23.5%)	10 (24.4%)	3 (-)	-
Cancer (n=6)	-	3 (2.9%)	2 (4.9%)	1 (-)	-
PTM* (n=2)	-	1* (1.0%)	1* (2.4%)	-	-
Thyroiditis (n=5)	-	5 (4.9%)	-	-	-

** PTM - papillary thyroid microcarcinoma*

compare relative indices χ^2 test was used; TIRADS effectiveness was evaluated by determining the sensitivity, specificity and accuracy of the method.

Results and Discussion

In total, 1033 patients aged from 17 to 82 years underwent operation because of TNs over the reported period. The USG conclusions in each observation were ranked according to the requirements of TIRADS scale and were assigned an appropriate grade of thyroid cancer risk (Fig. 1, 2).

It was not possible to stratify 385 (37.3%) cases according to TIRADS due to lack of information from USG description. There were absent certain characteristics, such as echogenicity, margins or structure; those cases were thus excluded from the survey. Therefore, in the subsequent analysis, 648 (62.7%) cases were considered, and those were divided into 2 groups: group I - "cystic thyroid nodules" - 164 (25.3%) patients; group II - "solid thyroid nodules" - 484 (74.7%) patients.

The average patients` age was 49.6±14.3 years. The average size of a solitary or dominant nodule was 29.9±14.1 mm. Thyroid cancer was diagnosed in 96 of 648 (14.8%) patients according to the histological examination.

Distribution by age, gender and thyroid status indexes in both groups did not differ significantly. However, the frequency of thyroid cancer was significantly different. So in group I, thyroid cancer was diagnosed in 6 cases (3.7%), and in group II - 90 cases (18.6%). The difference in thyroid cancer incidence was statistically significant (χ^2=21.655; p <0.00001). Consequently, it can be considered that there is a definite connection between cystic changes in TNs and the probability of their benign nature.

The next step was to analyse TIRADS scale effectiveness in predicting of thyroid cancer. A retrospective assessment of USG findings was made with appropriate stratification of thyroid cancer risk for both groups: cystic and solid thyroid nodules (Tab. 1, 2).

It was expected that the incidence of thyroid cancer increased with the risk group grade from TIRADS 2 to TIRADS 5. However, no CTN of the highest risk grade - TIRADS 5 was identified. It should also be noted that there is a difference in the incidence of PTM among cystic and solid nodules, 1.2% (2 from 164) vs. 3.5% (17 from 484). In order to determine TIRADS effectiveness in predicting thyroid cancer, high-risk groups of thyroid cancer TIRADS 4b and 5 were selected. Other groups - low-risk groups - TIRADS 2, 3 and 4a were used to compare [5]. Statistic data for both groups of patients (with solid and cystic nodules of the thyroid gland) were calculated (Tab. 3).

The TIRADS scale demonstrated a high

Table 2

Thyroid cancer risk stratification by TIRADS scale among solid nodules (n=484)

TIRADS (grade) Diagnosis	2 (n=0)	3 (n=222)	4a (n=169)	4b (n=83)	5 (n=10)
Colloid goiter (n=283)	-	157 (70.7%)	94 (55.6%)	30 (36.1%)	2 (-)
Adenoma (n=88)	-	43 (19.4%)	33 (19.5%)	11 (13.3%)	1 (-)
Cancer (n=90)	-	16 (7.2%)	33 (19.5%)	34 (41.0%)	7 (-)
PTM* (n=17)	-	8* (3.6%)	6* (3.6%)	3* (3.6%)	-
Thyroiditis (n=23)	-	6 (2.7%)	9 (5.3%)	8 (9.6%)	-

Table 3

TIRADS statistic data in predicting of thyroid cancer

Statistic	Cystic	Solid	p
Sensitivity	16.7%	45.6%	0.168
Specificity	93.0 %	86.8 %	0.038
Positive Predictive Value	8.3%	44.1%	0.018
Negative Predictive Value	96.7 %	87.5%	0.002
Accuracy	90.2%	79.1%	0.002

specificity of 93.0% in prediction of thyroid cancer in patients with CTN. At the same time, the sensitivity of TIRADS scale in detecting thyroid cancer in case of CTN remained low - 16.7%. Finally, in CTN evaluation, TIRADS showed a high overall diagnostic accuracy of 90.2%, but in practice it should be noted that the low level of positive predictive value of thyroid cancer among cystic nodules is 8.3%, especially when compared with solid nodules - 44.1%. Therefore, the low levels of positive predictive value and sensitivity significantly limit effectiveness of TIRADS in predicting cancer in CTN.

In general, the specificity, the negative predictive value and the overall accuracy of TIRADS in detection of cancer among cystic and solid thyroid nodules are approximately equal. A significant difference in TIRADS scale statistical data was observed in sensitivity between cystic and solid nodules: 16.7 and 45.6%, respectively; as well as positive predictive value - 8.3% and 44.1%. the statistic data showed that USG and TIRADS have certain limitations in prediction of thyroid cancer in patients with CTN compared with patients with solid thyroid nodules.

Conclusions

1. The TIRADS scale is an effective method for predicting cancer, especially among solid thyroid nodules.
2. The prevalence of cancer among cystic thyroid nodules is significantly lower compared to solid nodules: 3.7% vs. 18.6% (χ^2=21.655; p <0.00001).
3. The TIRADS scale sensitivity (16.7%) and positive predictive value (8.3%) in prediction of thyroid cancer are low in patients with cystic nodules, and therefore, cases of low risk of thyroid cancer, TIRADS 2-4a, require further precise follow up.

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