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# Value of sonographic, cytological and urgent histological tests in the oncological diagnostics of thyroid gland nodes

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**Background.** To evaluate thyroid cancer probability operating on follicular neoplasia.

**Materials and methods.** Retrospective examination of 86 patients that underwent surgery during the period 2000–2006 due to follicular neoplasia (n = 71) and suspected cancer (n = 15) diagnosed via fine needle aspiration biopsy of the thyroid gland. Sonography and intraoperative biopsy tests were performed. After the final histological test the patients were assigned to 2 groups: A – cancer of the thyroid gland (n = 24) and B – benign changes (n = 62).

**Results.** Hypoechogenic nodes of mononodal and multinodal goitre were typical for A group (p = 0.04). Cytological features for A group were: ruptures of cytoplasm through the nuclear membrane (4 out of 4 patients – 100%) (p = 0.06), inclusions of reddish colloid in the cytoplasm (4 out of 6 patients – 66.7%) (p = 0.34) and atypical cells (13 out of 25 patients – 52%) (p = 0.50). Out of 12 patients that had been diagnosed with cancer by the intraoperative biopsy test, the diagnosis was confirmed for 10 (83.3%), and benign changes were stated for 2 (16.7%) by final histological test.

**Conclusions.** Thyroid cancer was diagnosed both in the hypoechogenic mononadal and multinodal gland (p = 0.04). When follicular neoplasia was diagnosed by a cytological test, cancer of the thyroid gland was stated for 21.1% of patients by a histological test. Sensitivity of an intraoperative biopsy test was 55.6%, specificity was 93.1%.

**Key words:** follicular neoplasia, thyroid cancer, cytological test, intraoperative biopsy test

## INTRODUCTION

It is not feasible to differentiate follicular adenoma from cancer of the thyroid gland by fine needle aspiration puncture (FNAP) and cytological test. Follicular adenoma may be distinguished from carcinoma only by a histological test (1). Therefore if follicular neoplasia is diagnosed by FNAP and a cytological test, surgery is recommended (2).

Sensitivity of fine needle aspiration puncture (FNAP) technique with a cytological test in differentiation of cancer of the thyroid gland varies from 80% to 98%, specificity from 58% to 100% and general accuracy is 93% (3–7). As very different reliability of the results of FNAP and cytological tests is stated, we performed a retrospective overview of final histological tests of patients that were diagnosed with follicular neoplasma and suspected cancer of the thyroid gland by FNAP cytological test and defined more precisely the value of sonographic examination and urgent histological test for diagnosis of cancer of the thyroid gland.

## MATERIALS AND METHODS

Retrospective examination evaluating medical documents present in the case histories of 86 patients that underwent surgery in the tertiary level hospital Vilnius University Hospital Santariškių Klinikos during the period 2000–2006 due to follicular neoplasia (n = 71, mean age 51 years; 6 males and 65 females) and suspected cancer (n = 15, mean age 53 years; 3 males and 12 females) diagnosed via fine needle aspiration biopsy of the thyroid gland was performed. After surgery and final histological test the patients were assigned into 2 groups: A – cancer of the thyroid gland (n = 24; mean age 54.67 (±15.49) years, p = 0.221; 2 males and 22 females, p = 0.719) and B – benign changes (n = 62; mean age 49.98 (±13.73) years, p = 0.221; 8 males and 54 females, p = 0.719) (Table 1).

All 86 patients underwent sonographic examination of the thyroid gland before surgery to evaluate the presence of nodes, the size of nodes was measured for 59 patients (68.6%) and echogenicity was evaluated for 47 patients (54.6%). Intraoperative biopsy test (IBT) during surgery was performed for 47 patients (54.6%) out of 86 patients.

Diagnostic value of changes in the thyroid gland diagnosed by sonographic examination, PAAB cytologic changes and intraoperative biopsy test were established.

**Statistical analysis.** The data were analysed using SPSS software (version 11.5.0 for Windows operational system). Descriptive statistics is presented in the format mean value ± standard deviation. Average values of even variables were compared between groups for independent samples using t-test. If normality assumption was not satisfied, non-parametric Mann–Whitney test was used. To compare proportions in the frequency tables $\chi$ quadrate or Fisher exact test was used. Non-

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Table 1. **Demographic data of the patients**

| Data of the patients | Group A | Group B | p |
|---|---|---|---|
| Mean of age (± SD) | 54.67 ± 15.49 | 49.98 ± 13.73 | 0.221 |
| Sex | | | |
| Males | 2 | 8 | 0.719 |
| Females | 22 | 54 | 0.719 |

Table 2. **Results of sonographic examination of thyroid gland**

| Data of examination | A (n = 24) | B ( n = 62) | p |
|---|---|---|---|
| Echo structure n = 86 | n = 24 | n = 62 | |
| Single-nodded n = 25 | 9 | 16 | 0.208 |
| Multiple-nodded n = 61 | 15 | 46 | 0.208 |
| Size of nodes n = 59 | n = 14 | n = 45 | |
| ≤ 3 cm n = 41 | 11 | 30 | 0.311 |
| > 3 cm n = 18 | 3 | 15 | 0.311 |
| Echogenicity n = 47 | n = 10 | n = 37 | |
| Hypoechopgenic n = 17 | 7 | 10 | 0.040 |
| Isoechogenic n = 28 | 3 | 25 | 0.040 |
| Hyperechogenic n = 2 | 0 | 2 | 0.040 |

parametric Kruskal–Wallis test was used to compare more than two groups as sample volumes within the groups were small. Significance level in all tests was considered as equal to 0.05. Double-side values are presented everywhere as well.

## RESULTS

**Sonographic examination.** All 86 patients underwent sonographic examination of the thyroid gland before a surgery to evaluate the presence of nodes, the size of nodes was measured for 59 patients, and echogenicity was evaluated for 47 patients. Out of 24 patients of A group 9 (37.5%) were diagnosed with mononodal and 15 (62.5%) with multinodal goitre during sonographic examination. Hypothesis that there is a higher probability of cancer in the mononodal thyroid gland was not confirmed (p = 0.208). Echogenicity of the nodes of the thyroid gland was defined for 10 patients in A group and for 37 in B group. Out of 10 patients in A group hypoechogenic nodes were diagnosed for 7 patients (70%) and isoechogenic nodes for 3 patients (30%). Out of 37 patients in B group hypoechogenic nodes were diagnosed for 10 patients (27%), while isoechogenic nodes for 25 patients (67.6%), and hyperechogenic ones for 2 patients (5.4%). Cancer of the thyroid gland is diagnosed more often in hypoechogenic nodes (p = 0.04). The size of the nodes of the thyroid gland was measured for 14 patients in A group and for 45 patients in B group. Out of 14 patients in A group 11 (78.6%) were diagnosed with nodes up to 3 cm in diameter and 3 (21.4%) with bigger ones than 3 cm in diameter. Out of 45 patients of B group 30 (66.7%) were diagnosed with nodes up to 3 cm in diameter and 15 (33.3%) with those bigger than 3 cm in diameter. Hypothesis that cancer of the thyroid gland is diagnosed more often in nodes bigger than 3 cm in diameter was not confirmed (p = 0.311) (Table 2).

**PAAB and cytological test.** The most characteristic cytological features of cancer of the thyroid gland were defined: ruptures of cytoplasm through the nuclear membrane (4 out of 4 patients – 100%), inclusions of reddish colloid in the cytoplasm (4 out of 6 patients – 66.7%), papillary structures (4 out of 11 patients – 36.4%) and atypical cells (13 out of 25 patients – 52%). No single cytological change was statistically confirmed to be characteristic for cancer of the thyroid gland (p > 0.05) (Table 3). Out of 71 patients to whom cytologists suspected follicular neoplasia, cancer of the thyroid gland was diagnosed for 15 of them (21.1%). Out of 15 patients to whom cytologist suspected cancer of the thyroid gland this diagnosis was confirmed for 9 of them (60%). If follicular neoplasia signs or suspected cancer were diagnosed by a cytological test, after surgery cancer was diagnosed for 27.9% of patients.

**Intraoperative biopsy test.** IBT was performed for 47 patients. Cancer of the thyroid gland was stated for 12 patients (9 papillary, 1 follicular, 1 medullar and 1 Hurthle carcinomas), benign changes were found in 35 patients. Out of 12 patients that were diagnosed with cancer by IBT, diagnosis was confirmed for 10 of them (83.3%), and benign changes were stated for 2 of them (16.7%) by final histological test. Out of 35 patients that were diagnosed with benign changes by IBT, diagnosis was confirmed for 27 of them (77.1%), and cancer of the thyroid gland was diagnosed for 8 (22.9%) (Table 4).

Sensitivity, specificity, positive prognostic and negative prognostic values of IBT during surgery were calculated evaluating proportion of true positive (TP), true negative (TN), false positive (FP) and false negative (FN) data. Sensitivity of IBT during operations was determined using the following formula: TP/(TP + FN)*100% = 10/18*100% = 55.6%. Specificity of IBT during operations was determined using formula TN/(TN + FP)*100% = 27/29*100% = 93.1%. Positive prognostic value of IBT during operations was determined using formula TT/(TP + FN)*100% = 10/12*100% = 83.3%. Negative prognostic value of IBT during operations was determined by the following formula: N/(TN + FN)*100% = 27/35*100% = 77.1%. Sensitivity of intraoperative biopsy test is 55.6%, specificity is 93.1%, positive prognostic value is 83.3% and negative prognostic value is 77.1%.

Table 3. **Data of cytological test of the thyroid gland aspiration biopsy before surgery**

| Cytological changes | Group A (n = 24) | Group B (n = 62) | n |
|---|---|---|---|
| Nuclei of different size | 14 (33.3%) | 28 (66.7%) | 42 |
| Nuclei of uneven staining | 10 (31.3%) | 22 (68.7%) | 32 |
| **Atypical cells** | **13 (52%)** | **12 (48%)** | **25** |
| Microfollicular structures | 11 (28.9%) | 27 (71.1%) | 38 |
| Papillary structures | 4 (36.4%) | 7 (43.6%) | 11 |
| Irregular contours of nuclei | 9 (40.9%) | 13 (59.1%) | 22 |
| **Ruptures of cytoplasm through the nuclear membrane** | **4 (100%)** | **0 (0.00%)** | **4** |
| Young small nuclei | 4 (21.2%) | 26 (78.8%) | 30 |
| Hypertrophic nuclei | 6 (28.6%) | 15 (71.4%) | 21 |
| **Reddish inclusions in the cytoplasm** | **4 (66.7%)** | **2 (33.3%)** | **6** |
| Hurthle cells | 7 (19.4%) | 29 (80.6%) | 36 |
| Multinuclear gigantic cells | 6 (27.3%) | 16 (72.7%) | 22 |

**Note.** $p > 0.05$.

Table 4. **Diagnostic value of an intraoperative biopsy test during surgery (n = 47)**

| Conclusions of the intraoperative biopsy test | Group A (n = 18) | Group B (n = 29) | n |
|---|---|---|---|
| Cancer | 10 (83.3%) | 2 (16.7%) | 12 |
| Benign changes | 8 (22.9%) | 27 (77.1%) | 35 |

## DISCUSSION

Value of sonographic, cytological and intraoperative biopsy tests for diagnosis of the thyroid gland cancer was evaluated during the retrospective examination of patients that underwent surgery due to follicular neoplasia. Results of examination raise doubts on the earlier published statements that most often cancer of the thyroid gland is diagnosed in mononodal goitre. Based on our data multinodal goitre was diagnosed for 62.5% of all the patients. Other sources state that probability of cancer of the thyroid gland is similar in case of mononodal goitre and decreases if there is multinodal goitre (8, 9). There are sources confirming our results and stating that cancer is found more often in multinodal (35.1%) than in monodal thyroid (25.5%), however these data are not statistically reliable (10). Most of cancers of the thyroid gland are hypoechogenic ($p = 0.04$). Most of sources confirm this statement (11, 12). Other sources state that hypoechogenicity is not related to cancer of the thyroid gland (13).

It is not possible to distinguish follicular adenoma from follicular cancer by cytological test. A great amount of cells is characteristic to both adenoma and follicular cancer, microfollicular structures or trabeculae, enlarged and huddled together follicular cells, scanty colloid, spheres of reddish colloid are dominating. Follicular cancer is diagnosed by histological test when invasion of microfollicules into capsule or wall of blood vessels is diagnosed. When follicular neoplasia is diagnosed by cytological test, cancer of the thyroid gland during surgery is diagnosed for 21.1% of patients. Based on the data of other authors probability of cancer of the thyroid gland when follicular neoplasia is diagnosed varies from 6.9 to 30% (10, 14–16).

Cancer of the thyroid gland was not diagnosed by the intraoperative biopsy test in 16.7% cases and surgery ended with lobectomy. These patients had to be re-hospitalised and underwent reoperation in order to ablate the second lobe of the thyroid gland. Bibliographic sources confirm that routine intraoperative biopsy test during operation is important before making a decision to ablate entire thyroid gland thus avoiding reoperation (17).

The patient usually asks two questions when discussing with the surgeon the diagnosis of follicular neoplasia: what is the probability of cancer of the thyroid gland and if surgery is necessary? The easiest way for a patient to make a decision if statistical information is presented: if the cytologist diagnoses follicular neoplasia, cancer of the thyroid gland during surgery is stated for 21.1% of patients. If the cytologist suspects cancer of the thyroid gland, this diagnosis during surgery is confirmed in 60% of cases. Based on the data of other authors when cancer of the thyroid gland is stated by cytological test, the final diagnosis by histological test is confirmed in 95.5% of cases (10). It is necessary to explain the value of an intraoperative biopsy test and possible mistakes. In case of surgery to be performed due to single noded goitre and follicular neoplasia a surgeon may discuss with the patient the extent of operation with regards to patient's wishes: to ablate one lobe of the thyroid gland with suspected node and to perform an intraoperative biopsy test or, based on possible mistakes of an intraoperative biopsy test to ablate total thyroidectomy at once. Both options are acceptable.

## CONCLUSIONS

1. Cancer of the thyroid gland is diagnosed both in the mononadal and multinodal thyroid gland.

2. Cancer of the thyroid gland most often is diagnosed in hypoechogenic nodes ($p = 0.04$).

3. When follicular neoplasia is diagnosed by a cytological test, cancer of the thyroid gland has been stated for 21.1% of patients by histological test.

4. When cytological test indicates cancer of the thyroid gland, this diagnosis has been confirmed for 60% of patients by a histological test.

5. Sensitivity of an intraoperative biopsy test is 55.6%, specificity is 93.1%, positive prognostic value is 83.3%, and negative prognostic value is 77.1%.

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## ULTRAGARSINIO, CITOLOGINIO BEI SKUBAUS HISTOLOGINIO TYRIMŲ VERTĖ SKYDLIAUKĖS MAZGŲ ONKOLOGINĖJE DIAGNOSTIKOJE

*Santrauka*

**Tikslas.** Nustatyti skydliaukės vėžio tikimybę operuojant ligonius dėl folikulinės neoplazijos.

**Metodika.** Atliktas 86 pacientų, operuotų Vilniaus universiteto Santariškių klinikose 2000–2006 m., kai skydliaukės aspiracinės biopsijos plona adata metu buvo diagnozuota folikulinė neoplazija (n = 71) ir įtariamas vėžys (n = 15), retrospektyvinis tyrimas. Visi ligoniai tirti ultragarsu, operacijos metu atliktas skubus histologinis tyrimas. Po galutinio histologinio tyrimo ligoniai suskirstyti į dvi grupes: A – skydliaukės vėžys (n = 24) ir B – gerybiniai pokyčiai (n = 62).

**Rezultatai.** Skydliaukės vėžys diagnozuotas tiek vienmazgės, tiek ir daugiamazgės skydliaukės hipoechogeniškuose mazguose (p = 0,04). Būdingiausi skydliaukės vėžio citologiniai požymiai: citoplazmos išvaržos pro branduolio membraną (4 iš 4 ligonių – 100%; p = 0,06), rausvo koloido intarpai citoplazmoje (4 iš 6 ligonių – 66,7%; p = 0,34) ir atipinės ląstelės (13 iš 25 ligonių – 52%; p = 0,50). Galutinio histologinio tyrimo metu iš 12 pacientų, kuriems skubiu histologiniu tyrimu buvo nustatytas vėžys, 10 (83,3%) diagnozė patvirtinta, 2 (16,7%) diagnozuoti gerybiniai pokyčiai. Iš 35 ligonių, kuriems skubaus histologinio tyrimo metu diagnozuoti gerybiniai pokyčiai, 27 (77,1%) ligoniams diagnozė patvirtinta, 8 (22,9%) diagnozuotas skydliaukės vėžys.

**Išvados.** Skydliaukės vėžys diagnozuojamas ir vienmazgės, ir daugiamazgės skydliaukės hipoechogeniškuose mazguose. Citologinių pokyčių, būdingų tik skydliaukės vėžiui, nėra. Skydliaukės folikulinę neoplaziją ar vėžį galima diagnozuoti tik iš citologinių pokyčių komplekso. Citologinio tyrimo metu diagnozavus folikulinę neoplaziją, 21% ligonių po operacijos histologiniu tyrimu diagnozuotas skydliaukės vėžys. Skubaus histologinio tyrimo jautrumas – 55,6%, specifiškumas – 93,1.

**Raktažodžiai:** folikulinė neoplazma, skydliaukės vėžys, citologinis tyrimas, skubus histologinis tyrimas