

THYROID SCINTIGRAPHY. INCIDENCE OF THYROID CARCINOMA IN COLD NODE

Marko Krpan^{ID}, Bruno Rajič^{ID}, Marin Brajković^{ID}

University Clinical Hospital Mostar, 88 000 Mostar, Bosnia & Herzegovina

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SUMMARY

Introduction: Thyroid cancer is one of the most common malignant diseases of the endocrine system, and its changes are often asymptomatic in the early stages. Cold thyroid nodules are often suspicious and require further diagnostic testing to exclude a malignant character. Diagnostic methods such as scintigraphy, ultrasound, cytological puncture and pathohistological analysis are key to correctly distinguishing benign and malignant lesions. This paper analyzes the incidence of thyroid cancer in patients with cold nodules, with the aim of assessing the efficiency of different diagnostic methods in detecting malignant changes.

Objective: To assess the incidence of thyroid cancer in scintigraphically proven cold nodules.

Subjects and methods: The study included 98 patients who underwent thyroid scintigraphy in the period 2023-2024 due to suspected cold nodules. In all cases, additional diagnostic procedures were performed: ultrasound examination, aspiration cytology puncture and pathohistological analysis of tissue samples. Age, gender and diagnostic methods for determining the nature of the nodule were analyzed.

Results: Of the 98 patients, the majority of patients were between 60 and 79 years of age (43%). Women accounted for 78.6% of the subjects. The results showed that malignant thyroid carcinoma was diagnosed in 7.1% of the subjects. Cytology puncture showed high sensitivity (93%) and specificity (100%) in diagnosing benign and malignant lesions. The most common benign finding was follicular adenoma, while malignant changes were most often papillary carcinomas.

Conclusion: Scintigraphy, ultrasound and cytology puncture are key methods in the evaluation of cold thyroid nodules, with cytology puncture being the most sensitive for distinguishing benign from malignant lesions. The risk of malignancy in this study was 7.1%, with a higher proportion in men.

Keywords: Thyroid carcinoma, cold nodule, scintigraphy

Corresponding author: Marko Krpan, mag.rad.teh.; marko.krpanb@gmail.com

INTRODUCTION

Thyroid cancer is among the most common malignant diseases of the endocrine system, with a global incidence that is constantly increasing (1,2). Although many thyroid cases are benign, accurate diagnosis of malignant changes requires the use of various diagnostic methods (3). Cold thyroid nodules represent one of the most important diagnostic challenges, as they are asymptomatic and often go unrecognized until they become the cause of serious clinical problems (4,5). Cold nodules are nodules that do not show radioactive activity on thyroid scintigraphy, meaning that they do not behave like active nodules that typically take up radiopharmaceuticals (6). Therefore, these nodules often require further evaluation to exclude malignancy (7,8).

In the early stages, most cold thyroid nodules are benign, but the assessment of malignancy remains a challenge (9). Differentiation between benign and malignant changes in the thyroid gland requires the use of various diagnostic methods, including ultrasound, thyroid scintigraphy, cytological puncture, and histopathological analysis (10,11). Thyroid scintigraphy, which uses radiopharmaceuticals to record thyroid activity, is one of the key tools for identifying cold nodules (12). Ultrasound examination is an additional complementary method that allows visualization of the structure of the nodule and its characteristics, such as size, shape, and borders (13). Although these methods are very useful, the final diagnosis is often made by cytological puncture and histopathological analysis, which allow precise differentiation between benign and

malignant lesions (14,15). Thyroid biopsy is a minimally invasive procedure used to obtain tissue samples from a nodule and analyze them under a microscope. This method provides high sensitivity and specificity in detecting malignant changes, especially when used in combination with ultrasound. However, in certain cases, cytology may yield indeterminate results that require additional histopathological analysis for a definitive diagnosis (16). Histopathological processing of the tissue, which is performed after surgical removal of the nodule, provides a definitive answer about the malignancy and tumor type (17). Although the incidence of malignant thyroid nodules is relatively low, accurate diagnosis is essential to avoid inadequate treatment and to enable timely surgical removal of malignant lesions. Malignant thyroid cancer is most often diagnosed in the adult population, especially in older age, and women are more susceptible to the disease than men. There are also known genetic predispositions and risk factors such as a positive family history of thyroid disease, radiation exposure, and hormonal changes that increase the likelihood of developing malignancy (18).

The diagnosis of malignancy in thyroid cold nodules can be significantly improved by the correct choice of diagnostic procedures. This paper investigates the incidence of malignant changes in patients with scintigraphically proven thyroid cold nodules and evaluates the efficiency of different diagnostic methods in distinguishing benign and malignant lesions. Special focus is placed on the role of cytological puncture in establishing the diagnosis, as well as the need for further pathohistological analyses in cases of indeterminate cytological findings. Given

the increased prevalence of thyroid diseases, the aim of this study is to provide a clear picture of the incidence of malignant changes among patients with cold nodules, with an analysis of the role of each diagnostic procedure in the diagnostic process. The study also examines the influence of gender, age and other factors on the incidence of malignant nodules, which is crucial for improving clinical practice in early diagnosis and timely treatment of thyroid diseases.

OBJECTIVE OF THE RESEARCH

The aim of the study is to assess the risk of malignancy, the influence of clinical indicators on the risk of malignancy, and to investigate the distribution of cytological findings and pathohistological diagnoses in distinguishing benign from malignant lesions in a group of patients with ultrasound-proven solitary and scintigraphically proven "cold" nodules.

RESPONDENTS AND METHODS OF WORK

For the purposes of the study, a retrospective study was conducted at the Clinical Institute of Nuclear Medicine of the University Hospital in Mostar. The study covered the period from 2023 to 2024. The study included 98 patients, of whom 77 were women (78.6%) and 21 were men (21.4%), aged 10 to 89 years.

After thyroid scintigraphy, patients underwent additional diagnostic methods including ultrasound, aspiration cytological puncture, and laboratory tests of thyroid hormones. All patients with suspicious findings on scintigraphy, including those with indeterminate cytological results, underwent pathohistological analysis of thyroid tissue samples. The results were

analyzed in relation to gender, age, type of findings, and type of diagnostic procedure, and in particular the accuracy of cytological diagnosis compared to pathohistological findings was analyzed.

Scintigraphy

Thyroid scintigraphy was performed using 185 MBq of ^{99m}Tc-pertechnetate injected intravenously. Static imaging was performed 20 minutes after radionuclide administration. A single-head gamma camera with a 5 mm pinhole collimator was used to collect 200,000 pulses with an absorption maximum at 140-keV.

Cytological processing

Cytological samples were obtained by ultrasound-guided FNA method (Fine Needle Aspiration). The node was punctured, and the needle was withdrawn by aspirating the content of the node.

Pathohistological processing

After removing the node, pathohistological processing was performed. The cuts are routinely impregnated with paraffin, several cuts are made in different planes.

STATISTICAL ANALYSIS

Descriptive statistics were used for statistical analysis of data, including frequency and percentage distributions for basic demographic characteristics of the subjects (age, gender). To assess the association between diagnostic methods and findings, the χ^2 -test was used to analyze differences in the frequency of malignant and benign lesions among different groups (by gender and age) and the test to compare the sensitivity and specificity of cytological findings in

relation to pathohistological findings.

Statistical significance was set at $p < 0.05$.

Table 1. *Classification of changes according to cytological diagnosis*

Type of change	Cytological diagnosis
Benign changes	Nodular goiter
	Hashimoto's thyroiditis
	Pseudocystic change
Malignant changes	Papillary carcinoma
Unspecified changes	Cellular follicular change
	Follicular neoplasm
	Adenomatoid node
	Hurthle cell tumor

RESULTS

This section presents the demographic data of the subjects, the results of cytological and histopathological analysis, and the

overall incidence of carcinoma in cold thyroid nodules.

Table 2. *Distribution of respondents by age*

Age in years	Number of respondents	Share (%)
10-19	4	4,1
20-29	3	3,1
30-39	10	10,2
40-49	14	14,3
50-59	18	18,4
60-69	26	26,5
70-79	16	16,3
80-89	7	7,1
Total:	98	100

The age distribution of all subjects included in the study is shown. The

majority of patients are in the age range between 41 and 69 years.

Table 3. *Gender of respondents*

Respondent's gender	Number of respondents	Share (%)
Male	21	21,4
Female	77	78,6
Total:	98	100

The table shows the distribution of subjects with cold thyroid nodules by gender. A

higher prevalence of females was observed compared to males.

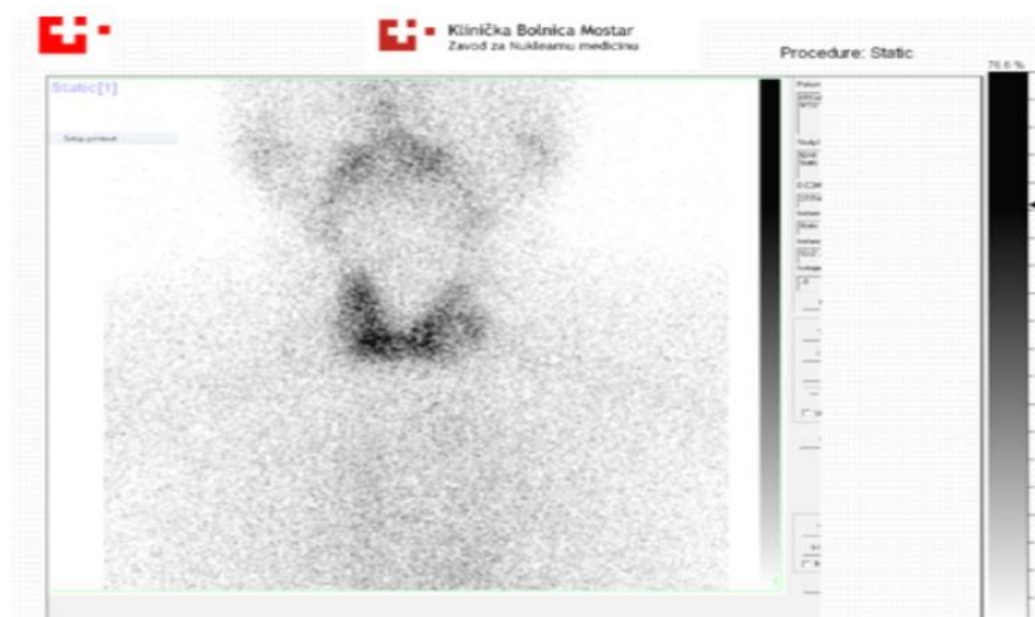


Figure 1. Static thyroid scintigram. Showing a cold nodule in a 69-year-old man.

Table 4. Distribution of cytological findings groups

Cytological finding group	Number of cases	Share (%)
Benign finding	52	53,1
Indeterminate finding	39	39,8
Malignant finding	7	7,1
Total	98	100

The table shows the distribution of cytological findings obtained by puncture of cold thyroid nodes. The majority of subjects had benign findings (53.1%), while malignant cytological findings were

determined in 7.1% of cases. Indeterminate findings, which include atypia and suspicious changes, accounted for 39.8% of all findings.

Table 5. Distribution of cytological findings

Cytological findings	Number of cases	Share(%)
Papillary carcinoma	7	7,1
Follicular neoplasm	19	19,5
Hashimoto's thyroiditis	2	2
Nodular goiter	40	40,1
Adenomatoid node	9	9,3
Hurthle cell adenoma	3	3,3
Pseudocyst	6	6,2
Thyocyte proliferation	12	12,5
Total	98	100

The table shows the detailed distribution of individual cytological diagnoses obtained by aspiration cytology of cold thyroid nodules. The most common finding was nodular goiter, present in 40.1% of cases.

Follicular neoplasm was recorded in 19.5% of subjects, while papillary carcinoma was detected in 7.1% of cases. Other findings included thyocyte proliferation (12.5%), adenomatoid nodule (9.3%), pseudocyst

(6.2%), Hurthle cell tumor (3.3%), and Hashimoto's thyroiditis (2%).

Table 6. *Distribution of cytological findings by gender*

Cytological finding group	Gender		Total
	Male	Female	
Benign finding	6	46	52
Indeterminate finding	8	31	39
Malignant finding	2	5	7
Total	21	77	98

The table shows the distribution of cytological findings by gender. Of the 98 patients, 77 (78.6%) were female and 21 (21.4%) were male. Benign findings were significantly more common in women (46

cases) than in men (6 cases). Indeterminate findings were recorded in 31 women and 8 men, while malignant findings were determined in 5 women and 2 men.

Table 7. *Distribution of pathohistological diagnoses (PHD)*

PHD	Number of cases	Share (%)
Nodular goiter	5	20,8
Follicular adenoma	11	45,8
Hurthle cell adenoma	2	8,3
Follicular carcinoma	1	4,2
Papillary carcinoma	5	20,9
Total	24	100

The table shows the distribution of histopathological diagnoses in 24 patients who underwent surgical treatment and histopathological analysis. The most common diagnosis was follicular adenoma,

present in 11 cases (45.8%), while papillary carcinoma and nodular goiter were recorded in 5 cases each (20.8% and 20.9%). Hurthle cell adenoma was diagnosed in 2 patients (8.3%), and follicular carcinoma in 1 patient (4.2%).

Table 8. *Distribution of pathohistological diagnoses (PHD) by gender*

PHD	Gender		
	Male	Female	Total
Nodular goiter	0	5	5
Follicular adenoma	3	8	11
Hürthle cell adenoma	1	1	2
Follicular carcinoma	0	1	1
Papillary carcinoma	1	4	5
Total	5	19	24

The table shows the distribution of histopathological diagnoses by gender of patients who underwent surgery. Of the 24 patients, 5 were male and 19 were female. The most common diagnosis in both sexes was follicular adenoma, with a total of 11 cases (3 males and 8 females). Papillary

carcinoma was recorded in 5 cases (1 male and 4 females), while all nodular goiters (5 cases) were diagnosed in females. Follicular carcinoma occurred in only one female patient, and Hürthle cell adenoma was evenly distributed between the genders (1 male and 1 female).

Table 9. Overall incidence of thyroid carcinoma in scintigraphically proven cold nodule

Tumor	Number of cases	Share (%)
Papillary carcinoma	6	6,1
Follicular carcinoma	1	1
Other diagnoses (benign)	91	92,9
Total	98	100

The table shows the overall incidence of malignant thyroid tumors in patients with a cold nodule confirmed by scintigraphy. Out of a total of 98 analyzed cases, a malignant tumor (carcinoma) was diagnosed in 7 patients, which accounts for 7.1% of the total sample. Among them, papillary carcinoma was found in 6 cases (6.1%), and follicular carcinoma in 1 case (1%). The remaining 91 cases (92.9%) were benign findings, indicating a high frequency of benign changes in cold nodules.

DISCUSSION

This study analyzed data from 98 patients with thyroid cold nodules with the aim of determining the incidence of malignant changes and comparing diagnostic methods, including scintigraphy, ultrasound, cytological puncture and pathohistological processing. The results showed that the incidence of malignant changes was 7.1%, which is in line with previous studies that indicate a risk of malignancy in cold nodules between 5% and 15% (3,5,9). These findings confirm that although the majority of cold nodules

are benign in nature, there is always a clinically significant risk of malignancy, which is why a multi-stage diagnostic approach is needed.

The age distribution of the subjects in our study showed that the largest number of patients belonged to the older age group, especially the group between 60 and 79 years, which is in line with literature data indicating an increased incidence of thyroid disease in the elderly population (7,12). It is interesting that, although malignant findings were most common between the ages of 40 and 79, no significant association between age and the risk of malignancy was established. This suggests that although age may be a risk factor for the development of thyroid disease in general, it is not a sufficiently specific predictor of cold nodule malignancy by itself.

Analysis by gender showed a significantly higher prevalence of women (78.6%), which is consistent with global epidemiological trends according to which women have a higher predisposition to thyroid diseases, which is explained by hormonal factors, genetic predispositions

and environmental influences (1,4,13). Our results further highlighted that, although women more often had benign changes, men had a relatively higher proportion of malignant findings. This fact suggests that cold nodules in men may require a higher level of clinical suspicion and more careful diagnostic evaluation.

Regarding diagnostic methods, the results confirm the key role of scintigraphy, ultrasound and especially cytological puncture. Cytological diagnostics in our study showed high sensitivity (93%) and specificity (100%), which is in line with previous studies that state that FNA (fine needle aspiration) represents the gold standard in the initial evaluation of thyroid nodules (9,16). In parallel, ultrasound plays an irreplaceable role in assessing the morphological features of the nodules and in selecting lesions for puncture, while scintigraphy allows for the differentiation of cold from warm nodules and thus determines the indication for cytological work-up. Final confirmation of the diagnosis, as in other studies, was possible only by pathohistological analysis, which remains the ultimate diagnostic authority (5,16).

The most common malignant type in our study was papillary carcinoma, which is consistent with the literature data describing it as the most common histological form of thyroid carcinoma (5). This concordance further confirms the consistency of our results with global trends and epidemiological data.

However, it is important to highlight the limitations of this study. This is a retrospective study with a limited number of subjects from a single clinical center, which may reduce the generalizability of the results to a wider population. Also, the analysis did not include all potential risk

factors, such as radiation exposure, dietary habits or family history, which could play a significant role in the occurrence of malignancy. Future studies with a larger number of patients, a multicenter approach and the inclusion of additional clinical and genetic parameters would enable a more comprehensive assessment of the risk and effectiveness of diagnostic methods.

Ultimately, the results of our study confirm that although the risk of malignancy in cold nodules is relatively low, the combination of scintigraphy, ultrasound and especially cytological puncture represents an optimal diagnostic approach. Special attention should be paid to men with cold nodules and the individualization of the diagnostic protocol according to the age and clinical characteristics of the patients. The systematic use of the above methods ensures timely detection of malignant lesions and optimizes the decision-making process in clinical practice.

CONCLUSION

Scintigraphy, ultrasound, and clinical examination are useful methods in the evaluation of thyroid cold nodules, but cytological puncture has been shown to be the most sensitive and specific in differentiating benign from malignant changes. In our study, the risk of malignancy was 7.1%, with papillary carcinomas being the most common form. Malignant findings were more common in men, while women had significantly more benign changes. The combination of multiple diagnostic methods remains the most reliable approach for the timely detection and treatment of malignant thyroid nodules.

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SCINTIGRAFIJA ŠTITNJAČE. POJAVNOST KARCINOMA ŠTITNJAČE U HLADNOM ČVORU

Marko Krpan^{ID}, Bruno Rajič^{ID}, Marin Brajković^{ID}
Sveučilišna klinička bolnica Mostar, 88000 Mostar, Bosna i Hercegovina

SAŽETAK

Uvod: Karcinom štitnjače predstavlja jednu od najčešćih malignih bolesti endokrinog sustava, a njegove promjene često su asimptomatske u početnim stadijima. Hladni čvorovi štitnjače su često suspekt i zahtijevaju daljnje dijagnostičko ispitivanje kako bi se isključio maligni karakter. Dijagnostičke metode poput scintigrafije, ultrazvuka, citološke punkcije i patohistološke analize ključne su za pravilno razlučivanje benignih i malignih lezija. Ovaj rad bavi se analizom incidencije karcinoma štitnjače u bolesnika s hladnim čvorovima, s ciljem procjene efikasnosti različitih dijagnostičkih metoda u otkrivanju malignih promjena.

Cilj: Procijeniti pojavnost karcinoma štitnjače u scintigrafski dokazanom hladnom čvoru.

Ispitanici i metode: U istraživanju je sudjelovalo 98 bolesnika koji su u razdoblju od 2023.-2024. godine podvrgnuti scintigrafiji štitnjače zbog sumnje na hladni čvor. U svim slučajevima provedeni su dodatni dijagnostički postupci: ultrazvučni pregled, aspiracijska citološka punkcija i patohistološka analiza uzoraka tkiva. Analizirani su dob, spol, te dijagnostičke metode za utvrđivanje prirode čvora.

Rezultati: Od 98 pacijenata, najviše bolesnika bilo je u dobi između 60 i 79 godina (43 %). Žene su činile 78,6 % ispitanika. Rezultati su pokazali da je maligni karcinom štitnjače dijagnosticiran u 7,1 % ispitanika. Citološka punkcija pokazala je visoku osjetljivost (93 %) i specifičnost (100 %) u dijagnosticiranju benignih i malignih lezija. Najčešći benigni nalaz bio je folikularni adenom, dok su maligne promjene bile najčešće papilarni karcinomi.

Zaključak: Scintigrafija, ultrazvuk i citološka punkcija ključne su metode u evaluaciji hladnih čvorova štitnjače, pri čemu je citološka punkcija najosjetljivija za razlikovanje benignih od malignih lezija. Rizik malignosti u ovom istraživanju iznosio je 7,1 %, s većim udjelom u muškaraca.

Ključne riječi: karcinom štitnjače, hladni čvor, scintigrafija

Autor za korespondenciju: Marko Krpan, mag. rad. teh.; marko.krpanb@gmail.com