ORIGINAL ARTICLE

Fine needle aspiration cytology in the diagnosis of thyroid nodules

Cytoponction à l'aiguille fine dans le diagnostic des nodules thyroïdiens

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Abstract

Introduction-Aim: Thyroid nodules are a frequent and mostly benign pathology. Failure to recognize a cancer remains a major concern for any physician confronted with this pathology. Fine needle aspiration cytology (FNAC) is the reference examination when managing thyroid nodules. The aim of our study was to evaluate the role of FNAC in determining the histological nature of thyroid nodules.
Methods: We conducted a cross-sectional, retrospective, and descriptive study, spread over a 5-year period from January 2016 to December 2020, carried out in our Department of Otolaryngology and Head and Neck Surgery.
Results: The median age of the 200 patients was 46 years. Female predominance was evident, with a sex ratio of 0.09. All our patients underwent FNAC followed by surgical excision. FNAC was non diagnostic in 8 cases (4%) and benign in 53 cases (20.50%). It revealed atypia of undetermined significance in 33 cases (16%), a follicular neoplasm in 45 cases (21.50%) and a malignant suspicion in 47 cases (22.50%). FNAC was malignant in 22 cases (10.5%). Pathological examination showed malignancy in 115 cases. FNAC has an overall sensitivity of 84% and a specificity of 71.6% in predicting thyroid nodules diagnosis.
Conclusion: Combining clinical and ultrasonographic criteria with cytological results improves the sensitivity of thyroid carcinoma screening.

Keywords: Thyroid nodule; Thyroid neoplasms; Thyroid Diseases; Ultrasound-Guided Fine Needle Aspiration

Résumé

Introduction-Objectif : Les nodules thyroïdiens sont une pathologie fréquente et majoritairement bénigne. Le risque de ne pas reconnaître un cancer reste une préoccupation majeure pour tout médecin confronté à cette pathologie. La cytoponction à l'aiguille fine (CPAF) est l'examen de référence dans la prise en charge des nodules thyroïdiens. L'objectif de notre étude était d'évaluer l'apport de la CPAF dans la détermination de la nature histologique des nodules thyroïdiens.
Méthodes : Nous avons mené une étude transversale, rétrospective et descriptive, sur une période de 5 ans, de janvier 2016 à décembre 2020, réalisée dans notre service d'Oto-Rhino-Laryngologie et de Chirurgie Cervico-Faciale.
Résultats : L'âge médian des 200 patients était de 46 ans. Une prédominance féminine était évidente, avec un sex-ratio de 0,09. Tous nos patients ont subi une CPAF suivie d'une exérèse chirurgicale. La CPAF était non contributive dans 8 cas (4 %) et bénigne dans 53 cas (20,50 %). Elle a révélé des atypies de signification indéterminée dans 33 cas (16 %), une néoplasie folliculaire dans 45 cas (21,50 %) et une suspicion de malignité dans 47 cas (22,50 %). La CPAF était maligne dans 22 cas (10,5 %). L'examen anatomopathologique a montré une malignité dans 115 cas. La CPAF présente une sensibilité globale de 84 % et une spécificité de 71,6 % dans la prédiction du diagnostic des nodules thyroïdiens.
Conclusion : La combinaison des critères cliniques et échographiques avec les résultats cytologiques améliore la sensibilité du dépistage du carcinome thyroïdien.

Mots-clés : Nodule thyroïdien ; Tumeurs thyroïdiennes ; Maladies thyroïdiennes ; Cytoponction

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What is known:
Thyroid nodules are mostly benign, and FNAC is a key diagnostic tool for distinguishing benign from malignant cases, guided by the Bethesda classification system.

What this article adds:
This study confirms FNAC's diagnostic accuracy (84% sensitivity, 71.6% specificity) and highlights the importance of combining clinical, ultrasound, and cytological data to improve thyroid cancer detection, while noting limitations in indeterminate cases.

Introduction

The thyroid nodule is a dystrophy developed within the gland. It mainly affects middle-aged women. Its clinical prevalence is estimated at between 4% and 7% [1]. Ultrasound prevalence is higher, ranging from 11 to 55%. Over 90% of nodules are benign, and cancer accounts for only 5-10% of cases. The difficulty lies in the fact that only histology can confirm or rule out malignancy. Fine-needle aspiration (FNA) plays a key role in determining the indication for surgery [2]. Since its introduction, up to 50% of nodules operated on have turned out to be malignant on histology. Ultrasound findings (EUTIRADS score) must be corroborated with clinical data before FNA is indicated [3]. The implementation of the Bethesda cytological classification has standardized diagnostic criteria, enabling decisions to be made according to precise recommendations. Our aim is to describe the contribution of cytology in determining the histological nature of thyroid nodules.

Methods

This is a cross-sectional, retrospective, descriptive study, over a 5-year period from January 1, 2016, to December 31, 2020. Adults with nodule(s) who underwent cervical ultrasound and FNA with cytological study and underwent surgery were included. Cases for which details of cytological and histological examination were not available were excluded. This study included 200 patients. On ultrasound, 291 nodules were objective. All nodules were scored according to the 5-category EU-TIRADS classification. Of these nodules, 208 meet the criteria of FNA which was done using ultrasound.
In our series, the indication for fine-needle aspiration (FNA) was based on the 2011 recommendations of the French Endocrinology Society, followed by the 2017 guidelines of the European Thyroid Association (ETA), as the study period spanned from 2016 to 2020.
Before 2017, FNA was systematically performed for all nodules larger than 2 cm. Nodules smaller than 7 mm were not eligible for FNA. For nodules measuring between 0.7 cm and 2 cm, FNA was indicated only in the presence of risk factors or suspicious ultrasound features. Since the introduction of the EU-TIRADS classification in 2017, FNA was performed in the following cases:
Nodules >10 mm classified as EU-TIRADS 5
Nodules >15 mm classified as EU-TIRADS 4 or 5
Nodules >20 mm classified as EU-TIRADS 3 to 5
Nodules >20 mm, regardless of their EU-TIRADS score, when associated with suspicious lymph nodes.
The various cytological results were classified according to the 2017 Bethesda classification into 6 groups.
There are six diagnostic categories for this system:
- Bethesda 1: Nondiagnostic or unsatisfactory.
- Bethesda 2: Benign.
- Bethesda 3: Follicular lesion of undetermined significance or atypia of undetermined significance (AUS).
- Bethesda 4: Follicular neoplasm, including oncocytic follicular neoplasm.
- Bethesda 5: Suspected malignancy.
- Bethesda 6: Malignant.
The indications for surgery were a plunging goiter, nodular size greater than 3 centimeters, suspicious nodules on ultrasound or cytological examination, signs of compression of neighboring structures, the patient's wish or carcinophobia.
Frozen section (FS) examination was systematically realized. The result was: benign, malignant, or differed to final histology examination.
To analyze the results of our study in terms of correlation between thyroid cytology findings and definitive histology, we eliminated non-diagnostic cytologies (Bethesda I) and indeterminate cytologies (Bethesda III and IV), as these categories cannot be classified either as benign due to the presence of cytological or architectural atypia, or as malignant because they do not meet the necessary criteria.
Subsequently, Bethesda II was considered as benign cytology and cytologies classified as Bethesda V and VI were grouped together as malignant cytology.
For FS, accuracy was determined in two ways, firstly by exclusion of differed result then by considering them as benign result as it doesn't affect the surgical decision.
Thus, the sensitivity, specificity, positive predictive value, and negative predictive value of FNAC and FS were calculated and compared.

Results

Our series consisted of 208 thyroid nodules collected from 200 patients. The median age was 46. Female predominance was noted, with a sex ratio of 0.09. The malignancy rate was higher in men (66.7%) than in women (57.5%). Regarding risk factors for thyroid cancer, none of the patients had undergone cervical irradiation during childhood. Fourteen patients had dysthyroidism, including 9 cases of hypothyroidism and 5 cases of hyperthyroidism. Six patients had a family history of goiter, two of them had dysthyroidism. No patient had a family history of thyroid cancer.
In terms of circumstances of discovery, the appearance of an anterior cervical swelling was the most frequent situation (65%), followed by chance discovery during a clinical or ultrasound examination by a physician in 28% of cases. Dysphagia was the reason for consultation in 4% of patients. Adenopathy was the circumstance of

discovery in 3% of cases.

Cervical ultrasound revealed 291 nodules, 208 of them had a FNAC. Ultrasound revealed multiple nodules in 67 patients (33.5%), and a solitary nodule in the remaining 133 patients. The mean nodule size was 22.31 mm. Six nodules were individualized for score 2, 51 nodules for score 3, 91 for score 4 and 60 for score 6.

The various cytological results were classified according to the 2017 Bethesda classification into 6 groups. It was non-diagnostic in 8 cases (4%) and benign in 53 cases (25,50%). It revealed atypia of undetermined significance in 33 cases (16%). A follicular neoplasm was noted in 45 cases (21,50%), and a malignant suspicion in 47 cases (22,50%). FNAC revealed malignancy in 22 cases (10,50%).

All patients were operated on. Initially, surgery consisted of loboisthmetomy in 85 cases. Total thyroidectomy was performed in 115 cases.

Second surgery for totalization following histological examination confirming malignancy was performed in 25 cases.

The response of the FS examination was in favor of malignancy in 56 cases, benignity in 70 cases, and was deferred in 82 cases.

Of the 208-thyroid nodule surgical specimens, the definitive histological examination revealed 93 benign nodules and 115 cases of thyroid cancer, distributed as follows (Table 1)

Table 1. Distribution of nodules by histological type

Histological type	Number	Percentage
NIFTP	1	0,48%
TBC	1	0,48%
Lymphocytic thyroiditis	49	23,5%
Thyroid adenoma	44	21,1%
Medullary carcinoma	1	0,48%
Oncocytic carcinoma	2	0,9%
Vesicular carcinoma	2	0,9%
Papillary carcinoma	110	52,8%

Comparing the result of FNAC to definitive histology showed various results which we resumed in table 2.

Table 2. BETHESDA classification and rate of malignancy

FNA results	Number	Malignancy percentage %
ND	8	12,5%
Benign	53	18,8%
AUS	33	66,6%
Follicular neoplasm	45	70%
Malignant suspicion	47	78,8%
Malignant	22	80%

We studied the performance of FNAC according to the histological type of thyroid carcinoma. (Table 3)

The results of FS were correlated with the definitive pathology (Table 4).

Table 3. Correlation between BETHESDA classification and histological type of carcinoma

	Type	Bethesda						
		I	II	III	IV	V	VI	Total
Papillary carcinoma	Classic	0	5	6	11	21	12	55
	Micro-carcinoma	1	0	6	4	9	8	28
	Papillary carcinoma with vesicular architecture	0	2	1	7	7	0	17
	Papillary carcinoma with oncocytic cells	0	0	1	5	1	1	8
	Diffuse sclerosing	0	0	0	1	1	0	2
	Vesicular carcinoma	0	1	1	0	0	2	
	Medullary carcinoma	0	0	0	0	1	1	
	Oncocytic carcinoma	0	2	0	0	0	2	

Table 4. Correlation between frozen section results and definitive histology

Frozen section	Definitive histology			
	Benign	Malignant	Total	Malignancy percentage
Benign	58	12	70	17%
Malignant	6	50	56	89%
Differed	29	53	82	64,6%
Total	93	115	208	

By correlating the results of the frozen section examination with the definitive histology, we were able to calculate the performance of this tool in predicting the risk of malignancy of thyroid nodules and to compare it to the FNAC performance (Table 5).

Table 5. Diagnostic performance of FS

Performance indices	Sensitivity	Specificity	Positive predictive value	Negative predictive value
FS (differed excluded)	82.85%	89.28%	90.62%	80.64%
FS (differed not excluded)	57.23%	89.28 %	93,54%	43.47%

We analyzed the characteristics of 115 malignant nodules on definitive anatomopathological examination, according to FNAC and frozen section examination (Table 6)

Table 6. Distribution of the different Bethesda categories according to the results of FS examination in the 115 malignant nodules.

FNAC results	Number of FNAC	Benign FS	Differed FS	Malignant FS	Total
Bethesda I	8	0	0	1	1
Bethesda II	53	1	7	3	9
Bethesda III	33	2	15	7	22
Bethesda IV	45	4	19	5	30
Bethesda V	47	5	12	18	37
Bethesda VI	22	0	0	16	16
Total	208	12	53	50	115

In the univariate analysis of predictive factors for thyroid nodule malignancy, several clinical and ultrasound features were significantly associated with malignancy.

These included age ≥40 years (p=0.017), presence of dysphonia (p=0.004), hard consistency on palpation (p=0.000), irregular margins (p=0.033), hypoechogenicity (p=0.048), presence of microcalcifications (p=0.011), and predominantly central vascularization (p=0.034). In contrast, sex (p=0.45), nodule size ≥2 cm (p=0.33), and presence of lymphadenopathy (p=0.079) were not statistically significant predictors. In the multivariate analysis of predictive factors for thyroid nodule malignancy, three variables were independently significant. Age was inversely associated with malignancy (OR = 0.958; 95% CI: 0.935–0.981; p=0.000), suggesting that younger age increases the risk. Dysphonia was a strong independent predictor (OR = 0.260; 95% CI: 0.098–0.686; p=0.007), as was hypoechogenicity (OR = 0.361; 95% CI: 0.162–0.804; p=0.013), both significantly associated with higher malignancy risk.

Discussion

Nowadays, cytology is an integral part in evaluating thyroid nodules [4]. It selects the 5% of subjects whose nodule is malignant. It is a minimally invasive, rapid, and reliable screening tool. Since its advent, the number of operations has fallen by 25 to 50%, while the incidence of cancers identified on an excisional specimen has risen to 30 or even 40% [5]. In fact, only 14% of resected thyroid nodules were histologically malignant prior FNA, whereas this proportion rises to 50% with FNAC [6,7].

New recommendations have emerged specifying the different indications for FNAC in thyroid nodules [7 - 9]. They are based on risk stratification of clinical and ultrasound malignancy. [10]

International and European societies recommend classifying FNAC findings according to the 2010 Bethesda cytological classification, revised in 2017 [11]. This ensures standardized management.

Cytology results can be divided into diagnostic, non-diagnostic and indeterminate cytologies.

Bethesda 1 non-diagnostic cytologies represent 5-10% of results, and correspond to hypocellular samples from cystic fluid, bloody samples or inadequate preparation [12]. In this category, the benign or malignant nature of the nodule cannot be estimated [11]. This category represents 4% of our series, 8 nodules of which only one was malignant on definitive histology.

Indeterminate cytologies are classified as Bethesda 3 and 4 and represent 10 to 20% of all results.

The Bethesda III category covers cellular atypia of undetermined significance; architectural and/or nuclear atypia that are neither sufficient to be classified as "suspicious of malignancy" or "malignant", nor clear enough to indicate that the nodule is benign. The estimated risk of cancer is of 5-15% [6]. Therefore, a second cytology at 3 months is recommended [12]. In our series, 16% of punctured nodules were Bethesda III class. Of these nodules, 66.6% were malignant and 33.4% benign on definitive histology.

Bethesda IV category: "Follicular neoplasm" and "Follicular oncocytic neoplasm" (FN/FON): This category includes nodules that could be vesicular or oncocytic carcinomas, to be referred for surgery, as their diagnosis is impossible via cytological examination and relies exclusively on demonstration of signs of vascular or capsular invasion that are only observed after histopathological study [12]. In principle, papillary carcinomas of vesicular architecture are not included in this category. However, nuclear criteria suggestive of papillary carcinoma are sometimes focal or discrete. All nuclear changes must therefore be carefully examined. In the presence of any nuclear change suggestive of papillary carcinoma, the lesion should preferably be classified as suspicious of malignancy or malignant [13].

This Bethesda category accounts for 21.5% of cases in our series. Of these nodules, 66% were malignant, while 33% were benign on definitive histology.

Molecular tests can be used to complete the assessment of the risk of malignancy, rather than proceeding directly to surgery. However, the sensitivity and specificity of these tests do not allow us to recommend their routine use [14].

Diagnostic cytologies include benign, suspicious, and malignant cytologies.

Benign cytology accounts for 60-70% of cases. It includes cysts, benign vesicular nodules, and Hashimoto's thyroiditis [12]. The risk of malignancy is estimated to be very low, in the order of 0 to 3% [11].

Regular checkup for 3 to 5 years is recommended, with an initial ultrasound examination within 6 to 18 months. If there are no changes, monitoring continues. In the event of significant radiological changes, a second puncture may be proposed. If the nodule increases in size, or in the presence of suspicious ultrasound criteria, surgical removal should be considered [15].

In our series, 25.5% of punctured nodules were benign on FNA. This was the most frequent category. Of these nodules, 83% were benign on definitive histology.

For the "malignancy suspect" or Bethesda 5 category, the diagnosis of malignancy is plausible but cannot be confirmed. This category covers all types of thyroid cancer, except for nodules suspected of being vesicular carcinoma or oncocytic carcinoma. These may be suspected papillary carcinoma, medullary carcinoma, lymphoma, metastasis or other. The risk of cancer is between 60% and 75% [11].

Overall, these cytologies represent 16% of cases in our series. This is in line with literature, where frequencies range from 5 to 23%.

Malignant cytology accounted for 5% of cases. All cytological criteria for malignancy must be present. The histological type of tumor must be explicitly mentioned in the report (papillary, medullary, anaplastic carcinoma, lymphoma, metastasis, etc.) [11].

In our series, of the 22 malignant cytologies (10.5%), 16 were found to be malignant on definitive histology.

Nevertheless, the contribution of FNA remains limited [14]. In fact, well-differentiated vesicular tumors cannot be detected by FNA, as their diagnosis is based on a set of non-cytological criteria (intravascular tumor emboli, rupture of the thyroid capsule, lymph node metastasis). On the other hand, micro-carcinomas discovered

incidentally during surgery on benign nodules cannot be detected by FNAC.

In the event of a non-contributory result from the first FNAC (insufficient cellularity or "atypia of undetermined significance (AUS)"), a second puncture should be performed within 3 to 6 months.

A second cytological determination may be indicated, usually 6 months to a year later, in the case of nodules with benign cytology, or in the case of any suspicious clinical or ultrasound changes and an increase in volume of more than 20% in one year. Another FNAC is also recommended in the event of discrepancies between ultrasound and FNA findings [16,17].

Given that less than 10% of thyroid nodules turn out to be malignant, fine needle aspiration should be considered as a screening test [17 - 19].

In a 1993 study by Gharib and Goellne of 18,183 FNAs, sensitivity and specificity were 83% and 92% respectively [19]. In another retrospective study of 4703 cases by Yang et al [20], the sensitivity of FNA was 94% and its specificity 98.5%. In another study by Wang et al [21], the diagnostic certainty of FNAC was 100% in the diagnosis of medullary and anaplastic carcinoma.

In our series, FNAC suggested malignancy in 53.3% of cases. It was concordant with the literature results, with a sensitivity of 90%, a specificity of 57.9%, a positive predictive value of 72% and a negative predictive value of 83%.

Conclusion

Nodular thyroid disease is a common condition, and in over 90% of cases is benign. The possibility of not recognizing a cancer is always worrying.

Fine-needle aspiration is the most effective complementary examination for its diagnostic and prognostic evaluation. It can be used to determine the malignant nature of a nodule based on several arguments, and to classify it according to the Bethesda classification. This classification harmonizes the presentation of results and provides the clinician with a quantification of the cytological risk of malignancy.

In the light of our study and review of the literature, we have been able to show that cytopuncture is a promising examination for the diagnosis, stratification and monitoring of thyroid nodules. A reassuring cytological examination can avoid unnecessary surgery in around two-thirds of nodules, but it should not be forgotten that some reassuring cytologies may include malignant carcinomas.

Close collaboration between the surgeon, radiologist and pathologist is therefore essential to improve the reliability of the cytological examination, minimizing discordant and delayed results.

References

1. Parsa AA. Epidemiology of thyroid nodules. In: Gharib H, dir. Thyroid nodules: diagnosis and management. Cham: Springer; 2018. p. 1-11.
2. Ferrer Soler C, Malacarne S. Nodules thyroïdiens bénins : quelle prise en charge en 2015 ? Rev Med Suisse. Jan 2016;12(500):32-4.
3. Haute Autorité de Santé (HAS). Exploration des pathologies thyroïdiennes chez l'adulte : pertinence et critères de qualité de l'échographie, pertinence de la cytoponction échoguidée [Internet]. Saint-Denis La Plaine: HAS; 2022
4. Charfi A, Bachraoui R, Meherzi S, Bahlouli M, Chahed H, Salah MB, et al. Apport de la cytoponction dans les cancers thyroïdiens. Journal Tunisien d'ORL et de Chirurgie Cervico-Faciale. Jun 2018;39:20-4.
5. Machała E, Sopiński J, Iavorska I, Kołomecki K. Correlation of fine needle aspiration cytology of thyroid gland with histopathological results. Pol PrzeglChir. 2018 Aug;90(6):1-5.
6. Cibas ES, Ali SZ. The bethesda system for reporting thyroid cytopathology. Am J Clin Pathol. 2009 Nov;132(5):658-65.
7. Delgrange MG. Intérêt de l'élastographie ShearWave pour la prise en charge des nodules thyroïdiens : étude Swethy : analyse intermédiaire [thesis : medicine]. Grenoble : Université Joseph Fourier; 2011.
8. Vitaux F. Irradiations de la thyroïde et cancers thyroïdiens : revue bibliographique critique. Sept Nucl Med. 2007;31(7):350-5.
9. Russ G, Royer B, Bigorgne C, Rouxel A, Bienvenu Perrard M, Leenhardt L. Prospective evaluation of thyroid imaging reporting and data system on 4550 nodules with and without elastography. Eur J Endocrinol. 2013 Apr;168(5):649-55.
10. Russ G, Bonnema SJ, Erdogan MF, Durante C, Ngu R, Leenhardt L. European thyroid association guidelines for ultrasound malignancy risk stratification of thyroid nodules in adults: the EU-TIRADS. EurThyroid J. 2017 Sep;6(5):225-37.
11. Cibas ES, Ali SZ. The 2017 bethesda system for reporting thyroid cytopathology. Thyroid. 2017 Nov;27(11):1341-6.
12. Hartl D. Les monographies amplifion- Du nodule au cancer thyroïdien. Updated May 2018 [Accessed January 26, 2023]. https://studenthouse.tn/carcinologie-medicale/409-atlas-d-anatomie-humaine.html
13. CochandPriollet B, Vielh P, Royer B, Belleannée G, Collet JF, Goubin Versini I, et al. Cytopathologie thyroïdienne : le système de Bethesda 2010. Ann Pathol. Jun 2012;32(3):177-83.
14. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 american thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the american thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016 Jan;26(1):1-133.
15. Durante C, Grani G, Lamartina L, Filetti S, Mandel SJ, Cooper DS. The diagnosis and management of thyroid nodules: a review. J Am Med Assoc. 2018 Mar;319(9):914-24.
16. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2006 Feb;16(2):109-42.
17. Illouz F, Rodien P, Saint André JP, Triau S, Laboureau Soares S, Dubois S, et al. Usefulness of repeated fine-needle cytology in the follow-up of non-operated thyroid nodules. Eur J Endocrinol. 2007 Mar;156(3):303-8.
18. Durante C, Grani G, Lamartina L, Filetti S, Mandel SJ, Cooper DS. The diagnosis and management of thyroid nodules: a review. J Am Med Assoc. 2018 Mar;319(9):914-24.
19. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med. 1993 Feb;118(4):282-9.
20. Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correlations. Cancer. 2007 Oct;111(5):306-15.
21. Wang M, Chen H, Wang Y, Lei J, Li Z. Diagnostic value and cost-effectiveness of FNA-CT versus FNAC for medullary thyroid carcinoma. Clin Endocrinol (Oxf). 2023 May;98(5):709-718. doi: 10.1111/cen.14852. Epub 2022 Nov 23. PMID: 36394172.