

Investigation of correlation between cytological and histological findings in suspected carcinoma of thyroid

Investigação da correlação entre achados citológicos e histológicos na suspeita de carcinoma da tireoide

Clarissa A. Brites^{1,2}; Ludmila B. S. Balsimelli^{1,2}; Karina M. P. A. Coelho^{1,3}; Hercílio Fronza-Júnior²; Jaqueline Stall^{2,3}; Paulo Henrique C. França³

1. Hospital Municipal São José, Santa Catarina, Brazil. 2. Centro de Diagnósticos Anatomopatológicos (CEDAP), Santa Catarina, Brazil.

3. Universidade da Região de Joinville (UNIVILLE), Santa Catarina, Brazil.

ABSTRACT

Introduction: The thyroid cytopathologic classification based on The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) standardized results derived from fine-needle aspiration (FNA). It has facilitated communication among clinicians, seems to reduce the number of unnecessary thyroidectomies and also improves the quality of malignancy detection. **Objective:** To evaluate the correlation between cytopathological samples classified according to TBSRTC and their histological finding after specimen examination following surgical procedure. **Methods:** Cytopathological samples classified according to TBSRTC were correlated with the respective anatomopathological finding after thyroidectomy. There were retrospectively included all cases of thyroidectomy with previous FNA in the same lateral position of the organ that occurred within two years. **Results:** The 200 cases of thyroid FNA analyzed were distributed in 25 nondiagnostic or unsatisfactory cases (I; 12.5%), 45 benign cases (II; 22.5%), 48 atypia or follicular lesions of undetermined significance [(AUS/FLUS), III; 24%], 23 suspected cases for follicular neoplasia or follicular neoplasias [(SFN/FN), IV; 11.5%], 40 cases suspected for malignancy (V; 20%), and 19 malignant cases (VI; 9.5%). The malignancy rates observed for categories I to VI were 12%, 13.3%, 29.2%, 43.5%, 85%, and 100%, respectively. **Conclusion:** The prevalence of Bethesda II category was lower than predicted by TBSRTC (60%-70%), as well as Bethesda III was higher than recommended (7%). Nevertheless, the corresponding malignancy rates were within the expected ranges.

Key words: biopsy fine-needle; thyroid gland; carcinoma.

INTRODUCTION

Thyroid carcinoma is the commonest malignant neoplasm of the endocrine system, accounting for 1%-2% of all malignant neoplasms in humans, being more frequent in women in an approximate ratio of 3:1^(1, 2). Studies have shown a worldwide increasing incidence trend, perhaps due to improvements in the detection of small tumors⁽¹⁾. Thyroid nodules are very common in the general population and, although suspected for carcinoma, only 5% are actually malignant^(2, 3).

Nodules smaller than 1 cm of maximum diameter are usually not biopsied unless exhibiting suspected ultrasound characteristics, such as microcalcifications, or if accompanied by other risk factors that increase suspicion of malignancy, such as history of head

and neck radiation, family history of thyroid disease, presence of lymphadenopathy, female patient, and Asian ancestry^(2, 3).

Fine-needle aspiration (FNA) of nodules in the thyroid gland followed by cytological evaluation, especially ultrasound guided one, is considered the gold standard for the differential diagnosis due to its simplicity of execution, safety, cost-effectiveness and diagnostic accuracy⁽⁴⁾. According to Huang *et al.* (2015)⁽¹⁾, FNA shows sensitivity and specificity of approximately 83% and 92%, with false negatives varying from 1% to 21%, emphasizing that these rates may be technician-dependent. Therefore, diagnostic discrepancies are not uncommon.

The thyroid cytopathologic classification based on The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), introduced in 2007, standardized results derived from FNA and

has facilitated communication among clinicians, reducing the interobserver variability of this procedure⁽⁴⁾. It establishes six diagnostic categories and attributes risk of malignancy, adding recommendations for each category as well⁽⁴⁾. Studies have shown that the use of TBSRTC reduces the number of unnecessary thyroidectomies and also improves the quality of malignancy detection⁽³⁾.

The objective of this study was to evaluate the correlation of cytopathological interpretation classified according to TBSRTC with histological findings of the specimen examination after surgical procedure.

METHODS

This cross-sectional retrospective study was performed based on database from XXX, located in Joinville, southern Brazil. There were collected cytological and histological data from all patients with previous FNA to thyroidectomy between May 2013 and May 2015. There were excluded cases of thyroidectomy without previous FNA or with FNA in a lobe not corresponding to that of thyroidectomy. The cytological result of FNA, according to TBSRTC, was correlated with the histopathological report after thyroidectomy. Data were analyzed using descriptive statistics.

This study was approved by the Research Ethics Committee of the Hospital Municipal São José under protocol no. 2171978.

RESULTS

There were analyzed 200 cases of thyroid FNA classified according to TBSRTC. Most of the results were contained in Bethesda III category (24%) (**Table 1**).

The correlation of the diagnoses derived from FNA with the histopathological examination of the resected specimens is shown in **Table 2**. Among the cases classified as Bethesda II, six (13.3%) were malignant lesions at the histological examination, being all of these diagnosed as papillary carcinomas, and one corresponding to the follicular variant. Among the 83 patients with malignancy diagnosis confirmed at the histopathological examination, 77 had been classified as Bethesda III or higher category on previous cytological examination. Therefore, the sensitivity and specificity of this test was 93% and 42%, respectively.

DISCUSSION

In the present study, the prevalence of cases classified in diagnostic category III (24%) was higher than that predicted by TBSRTC (7%), as well as higher than prevalence rates (0.8% to 18.8%) identified in other studies⁽⁵⁻⁷⁾. This category has generated controversy due to the inconsistent use among different institutions and should be used as a last resort⁽⁶⁾. The malignancy rate observed

TABLE 1 – Distribution of diagnoses derived from thyroid FNA according to TBSRTC categories and corresponding malignancy rates observed in the histological analysis

TBSRTC	Diagnostic category	Prevalence (%)	Malignancy rate [% (n/N)]
I	Nondiagnostic or unsatisfactory	12.5	12 (3/25)
II	Benign	22.5	13.3 (6/45)
III	Atypia or follicular lesion of undetermined significance	24	29.2 (14/48)
IV	Suspected for follicular neoplasm or follicular neoplasm	11.5	43.5 (10/23)
V	Suspicious for malignancy	20	85 (34/40)
VI	Malignant	9.5	100 (19/19)

FNA: *fine-needle aspiration*.

TBSRTC: *The Bethesda System for Reporting Thyroid Cytopathology*.

TABLE 2 – Correlation between cytological (FNA) and histological diagnoses of the thyroid

TBSRTC	Histopathological diagnoses (n)					
	Non neoplastic	Follicular adenoma	Hürthle cell adenoma	Follicular carcinoma	Papillary carcinoma	Anaplastic carcinoma
I	20	2	0	1	2	0
II	35	3	1	0	6	0
III	28	2	4	2	12	0
IV	9	1	3	2	8	0
V	5	0	1	1	33	0
VI	0	0	0	0	17	2

FNA: *fine-needle aspiration*; TBSRTC: *The Bethesda System for Reporting Thyroid Cytopathology*.

in our study (29.2%) was in the range reported in other studies (5% to 69%)^(7,8). It is recognized a great variation in the malignancy rates in the Bethesda III category among different institutions and among cytopathologists of the same institution, depending on where they have received training in cytopathology⁽⁹⁾. In our study, most of the malignant lesions in this category were diagnosed as papillary carcinoma (12/14; 85.7%), an equivalent result (86.8%) as described by Ho *et al.* (2014)⁽⁶⁾ in patients with thyroid nodules classified according to TBSRTC between 2008 and 2011 at the Memorial Sloan-Kettering Cancer Center, in New York. A second opinion is indicated for the accurate diagnosis through FNA in cases classified in this category, since it is considered subjective and not homogeneous^(5,9). It is suggested that cases with focal nuclear atypia have a higher risk of malignancy and should be classified as Bethesda V⁽⁹⁾.

On the other hand, the prevalence of Bethesda II results (22.5%) was lower than that predicted by the same system (60%-70%), as well as lower than in other studies (40%-87.5%)⁽⁵⁻⁸⁾. Park *et al.* (2014)⁽¹⁰⁾, who also observed a lower than expected percentage in this category, state that a possible reason is the fact that many patients already presenting clinical suspicion of thyroid carcinoma were referred from other health care services for confirmation purposes of the diagnostic hypothesis by FNA. All malignant cases confirmed in the histological analysis corresponded to papilliferous carcinomas, which was also observed by Park *et al.* Other studies have shown histopathological diagnoses ranging from no malignant cases to diagnoses such as papillary carcinoma, follicular carcinoma, medullary carcinoma, and lymphoma^(4, 5, 7, 8, 11). Günes *et al.* (2015)⁽¹²⁾ reported that, in false-negative cases in FNA, the interpretive diagnostic error was particularly severe in “gray-zone” of follicular adenomas, follicular variant of papillary carcinomas, and papillary carcinomas with cystic change.

Garg *et al.* (2015)⁽⁷⁾ and Arul *et al.* (2015)⁽⁸⁾ compared their findings with different studies regarding the distribution of cases

and malignancy rates according to categories of the TBSRTC. These results were compared with ours and are shown in **Table 3**. The malignancy rates identified in the present study were similar to those found in other studies across all diagnostic categories.

The cases corresponding to category Bethesda I are more likely to present benign than malignant histology, as was identified in our study (Table 1) and described by Yang *et al.* (2007)⁽¹³⁾ and Yassa *et al.* (2007)⁽¹⁴⁾ (10.7% and 10% of malignancy rates, respectively)^(8,9). However, as reported by Arul *et al.* (2015)⁽⁸⁾, the prevalence of malignancy observed in Bethesda I may vary considerably (from 0% to 35.3%) and also a large number of patients in this category are not submitted to surgery, which may influence the observed rates⁽⁸⁾.

Among the malignant cases belonging to Bethesda IV category in our study, 80% corresponded to papillary carcinomas and 20% to follicular carcinomas on subsequent histopathological examination, which are results similar to those reported by Guo *et al.* (2017)⁽⁵⁾ (75% papillary carcinoma and 25% follicular carcinoma).

In regard to the Bethesda V category in our study, 94.3% were papillary carcinomas. Differently, Garg *et al.* (2015)⁽⁷⁾ reported that their three cases in this category corresponded to medullary carcinoma, follicular adenoma, and follicular carcinoma at the histological examination, with no papillary carcinoma. Finally, all Bethesda VI cases were confirmed as malignant lesions, as expected. The majority corresponded to papillary carcinomas (89.5%), which was also described by Garg *et al.*

The sensitivity observed in the present study (93%) was also similar to that of Garg *et al.* (88.9%), while the specificity was different (42% vs. 84.3%). When evaluating other studies, they showed the sensitivity of thyroid FNA ranged from 76.92% to 100% and the corresponding specificity between 64.6% and 98.5%⁽⁷⁾. The retrospective design and relatively small number of cases, as well as the fact that the diagnoses, both cytopathological and

TABLE 3 – Comparison between the rates of malignancy and prevalences in each diagnostic category recommended by TBSRTC observed in the present study and described by other authors

TBSRTC	Prevalence (%)			Malignancy rate (%)	
	Recommended	Present study	Other studies ^a	Present study	Other studies ^a
I	< 10	12.5	1.18 to 28.9	12	0 to 35.3
II	60-70	22.5	40.6 to 87.5	13.3	0 to 16
III	< 7	24	0.8 to 18.8	29.2	5 to 69
IV	N/A	11.5	0.4 to 16.1	43.5	14 to 50
V	N/A	20	1.3 to 19.3	85	53 to 98.7
VI	3-7	9.5	0.9 to 17.3	100	94 to 100

TBSRTC: The Bethesda System for Reporting Thyroid Cytopathology; N/A: not applicable; ^aGarg *et al.* (2015) and Arul *et al.* (2015)^(7,8).

histopathological, were performed by different pathologists, may also have contributed as relevant limitations of this study.

CONCLUSION

We concluded that the cyto-histological correlation of the diagnoses evaluated in this study is in accordance with the current literature, although the prevalence of Bethesda II category was lower and Bethesda III category was higher than

that recommended by TBSRTC. It is believed that the presence of pathologists while the FNA is being done may positively influence the diagnostic accuracy allowing a better correlation among clinical, imaging and cytological data.

DISCLOSURE STATEMENT

No funding was received for this study. The authors declare no conflicts of interest.

RESUMO

Introdução: A classificação citopatológica tireoidiana com base no Sistema de Bethesda para Relatos de Citopatologia da Tireoide (SBRCT) padronizou os resultados provenientes de punção aspirativa por agulha fina (PAAF). Seu uso tem facilitado a comunicação entre clínicos, parece reduzir o número de tireoidectomias não necessárias e também melhora a qualidade na detecção de malignidade. **Objetivo:** Avaliar a correlação entre amostras citopatológicas classificadas de acordo com o SBRCT e seu achado histológico após análise da amostra pós procedimentos cirúrgico. **Métodos:** Amostras citopatológicas classificadas de acordo com Sistema de Bethesda foram correlacionadas com o achado anatomopatológico respectivo após tireoidectomia. Foram incluídos todos os casos de tireoidectomia com PAAF anterior, na mesma lateralidade do órgão, ocorridos no período de dois anos. **Resultados:** Os 200 casos de PAAF de tireoide analisados foram distribuídos em 25 casos não diagnósticos ou insatisfatórios (I; 12,5%), 45 casos benignos (II; 22,5%), 48 atípias ou lesões foliculares de significado indeterminado [(AUS/FLUS), III, 24%], 23 casos suspeitos para neoplasia folicular ou neoplasias foliculares [(SFN/FN), IV; 11,5%), 40 casos suspeitos para malignidade (V; 20%) e 19 casos malignos (VI; 9,5%). As taxas de malignidade observadas para as categorias I a VI foram 12%, 13,3%, 29,2%, 43,5%, 85% e 100%, respectivamente. **Conclusão:** A prevalência da categoria II de Bethesda foi menor do que a recomendada pelo SBRCT (60%-70%), bem como a categoria III, a qual foi maior do que a recomendada (7%), porém os índices correspondentes de malignidade encontraram-se dentro das variações esperadas.

Unitermos: biópsia por agulha fina; glândula tireoide; carcinoma.

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CORRESPONDING AUTHOR

Clarissa Almeida Brites

Centro de Diagnósticos Anatomopatológicos (CEDAP); Rua Mário Lobo St, 61; CEP: 89201-330; Joinville-SC, Brasil; Phone: +55 (47) 3422-9607; Fax: +55 (47) 3433-9499; e-mail: clabrites@hotmail.com.



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