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ORIGINAL ARTICLE

Sensitivity and specificity of the transoperative histopathological study compared to definitive histopathological report in patients with thyroid nodule TIRADS 4 and 5

Sensibilidad y especificidad del estudio histopatológico transoperatorio comparado con el reporte histopatológico definitivo en pacientes con nódulo tiroideo TIRADS 4 y 5

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Abstract

Introduction: *Thyroid cancer is the most common endocrine malignancy, and survival is 98%. Incidence drops by 2.5% annually as newer criteria are used to diagnose it. Fine-needle aspiration biopsy is used in the initial evaluation to obtain a sample. The transoperative histopathological study has an efficacy of > 97% and helps to avoid unnecessary dissections. The diagnostic gold standard is the definitive histopathological study.* **Objective:** *The objective of this study was to determine the sensitivity and specificity of the transoperative histopathologic study of the thyroid compared to the definitive histopathologic report in patients with thyroid imaging reporting and data system (TIRADS) 4 and 5.* **Materials and methods:** *This study was observational, comparative, cross-sectional, and homodemographic study in patients who underwent hemithyroidectomy surgery and who underwent a transoperative study during the years 2021 and 2022. Descriptive statistics were used, and the results were compared with the definitive histopathological study.* **Results:** *There were 46 patients (five males and 46 females), mean age 47.35 ± 13.83 years (range: 22-70), and sex ratio female > male (8:1). The transoperative study, for TIRADS 4, has a sensitivity of 58.3% and a specificity of 95.4%, with a positive predictive value (PPV) of 87.5% and negative predictive value (NPV) of 80.7%; and for TIRADS 5, a sensitivity of 83.3% and a specificity of 100%, with PPV of 100% and NPV of 85.7%.* **Conclusions:** *Transoperative study in patients with advanced-stage thyroid nodule TIRADS 5 has a better sensitivity and specificity than in the other previous stages.*

Keywords: *Thyroid Cancer. Surgery. Transoperative. Sensitivity. Specificity.*

Resumen

Introducción: *El cáncer de tiroides es la neoplasia maligna endocrina más común y su supervivencia es del 98%. La incidencia baja un 2.5% anualmente ya que se utilizan criterios más nuevos para diagnosticarlo. La biopsia por aspiración con*

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aguja fina se utiliza en la evaluación inicial para la obtención de una muestra. El estudio histopatológico transoperatorio tiene una eficacia > 97% y ayuda a evitar disecciones innecesarias. El método diagnóstico de referencia es el estudio histopatológico definitivo. **Objetivo:** *Determinar la sensibilidad y la especificidad del estudio histopatológico transoperatorio de tiroides en comparación con el reporte histopatológico definitivo en pacientes TIRADS 4 y 5.* **Método:** *Estudio observacional, comparativo, transversal y homodémico en pacientes operados de hemitiroidectomía a quienes se realizó estudio transoperatorio durante los años 2021 y 2022. Se utilizó estadística descriptiva y se compararon los resultados con el estudio histopatológico definitivo.* **Resultados:** *Fueron 46 pacientes (5 hombres y 46 mujeres), edad media 47.35 ± 13.83 años (rango: 22-70), relación por sexo mujer > hombre (8:1). El estudio transoperatorio, para TIRADS 4, posee una sensibilidad del 58.3% y una especificidad del 95.4%, con un valor predictivo positivo (VPP) del 87.5% y un valor predictivo negativo (VPN) del 80.7%; y para TIRADS 5, una sensibilidad del 83.3% y una especificidad del 100%, con un VPP del 100% y un VPN del 85.7%.* **Conclusiones:** *El estudio transoperatorio en pacientes con nódulo tiroideo en estadios avanzados TIRADS 5 posee unas mejores sensibilidad y especificidad que en los demás estadios previos.*

Palabras clave: *Cáncer de tiroides. Cirugía. Transoperatorio. Sensibilidad. Especificidad.*

Introduction

The past three decades have witnessed a constant increase in the incidence of thyroid cancer worldwide[1,2]. It is diagnosed at an earlier age compared to most other cancers affecting adults[2]. Women are 3 times more likely to develop thyroid cancer than men[2,3]. Figures from the European Network of Cancer Registries show estimate incidence rates in women that are approximately 3 times higher versus men[4]. Although rates vary from one country to another; in Mexico, it is estimated that around 35% of the population will have a thyroid nodule at some point in their lives, and approximately 10% of them will exhibit some form of thyroid cancer[5].

Thyroid cancer originates from follicular epithelial cells or parafollicular C cells. Derived from follicular cells, thyroid cancer is categorized into four histological types: papillary thyroid cancer (80-85%), follicular thyroid cancer (10-15%), poorly differentiated thyroid cancer (< 2%), and anaplastic thyroid cancer (< 2%)[6,7].

Less invasive alternatives to surgery for treating low-risk thyroid cancer, such as active surveillance and minimally invasive interventions, are being explored[8,9]. Ultrasound-guided fine-needle aspiration biopsy (FNAB) is the preferred technique for evaluating thyroid nodular disease due to its ease of performance, diagnostic yield, and minimal complications[10]. The most significant setback of FNAB is the amount of non-diagnostic punctures due to insufficient or hemorrhagic material[11,12].

Intraoperative frozen section (IFS), when used correctly, provides important information; however, it is not useful when a definite cytological diagnosis is already available, although its performance varies depending on each particular circumstance[13]. When the diagnosis has not been established before surgery or in suspected cases of benign lesions where the possibility of malignant neoplasms has not been excluded, the specimen is generally examined with frozen section cuts to determine the need for more extensive surgery intraoperatively[14].

When the pre-operative diagnosis is suspicious for papillary carcinoma (Bethesda VI), the IFS has a 100% positive predictive value (PPV) and a 50% negative predictive value (NPV), facilitating the decision to complete total thyroidectomy. In the latter circumstance, the IFS results in an adequate cost-effectiveness ratio; yet, PPV and NPV may vary from one center to the other depending on the prevalence of malignancy[15].

Therefore, the utility of available diagnostic tools in the individualized context of each patient should be established, as well as the optimal use of institutional resources, thereby improving diagnostic certainty, guiding clinical judgment, and the treating physician's decision-making.

The reference diagnostic method is the definitive histopathological examination performed after surgical removal of the thyroid gland[16].

The objective of this study was to determine the sensitivity and specificity of IFS compared to definitive histopathological examination in patients with thyroid imaging reporting and data system (TIRADS) 4 and 5 thyroid nodules.

Materials and methods

This study was sensitivity and specificity study of a diagnostic test. Patients > 16 years, of both sexes, diagnosed with thyroid nodules (TIRADS 4 and 5) and undergoing hemithyroidectomy with IFS from June 2021 to June 2022 at a tertiary referral center from Mexico were included in the study.

A review of the surgical schedule of the surgical oncology service was conducted, including patients diagnosed with thyroid nodules who underwent hemithyroidectomy

with IFS, and data collection was supplemented with records from the clinical archive and outpatient clinic. Patients whose studies recorded in the health records could not be evaluated or were incomplete were excluded from the study. Patients with indeterminate or inconclusive results were excluded as well.

Data analysis was performed using descriptive statistics. Frequencies and percentages were calculated for non-parametric variables, and measures of central tendency and dispersion (mean, median, mode, minimum, maximum, and standard deviation) for the parametric ones. Sensitivity, specificity, PPV, NPV, and the efficacy of IFS in TIRADS 4 and 5 were determined using the Statistical Package for the Social Sciences 29 statistical processor.

The study was approved by the Local Research and Ethics in Health Research Committee. All participants signed the informed consent letter, and their anonymity was preserved at all times. Data were used solely for scientific purposes.

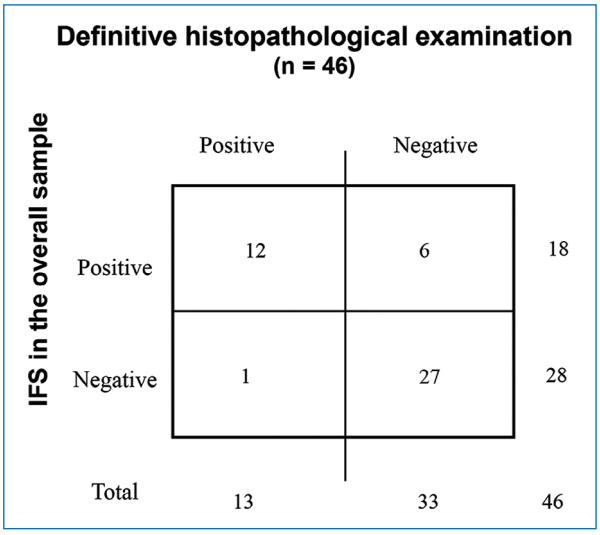

Figure 1. Sensitivity and specificity of intraoperative frozen section in thyroid imaging reporting and data system four and five patients versus the definitive histopathological examination. Sensitivity: 92.3%; specificity: 81.8%; positive predictive value: 66.6%; negative predictive value: 96.4%; and accuracy: 84.7%.

Results

A total of 46 patients were recruited, with a mean age of 47.35 years ± 13.83 years (range, 22-70) and a female-to-male ratio of 8.2:1. Regarding thyroid function, most (71.7%) were euthyroid, followed by hypothyroidism (26.1%) and hyperthyroidism (2.2%). The right side (69.6%) predominated over the left one (30.4%). According to TIRADS classification, the following frequencies were found: 73.9% were TIRADS 4, and 26.1% were TIRADS 5. Benign histological lineage prevailed over malignant.

In both TIRADS 4 and 5 groups, the IFS versus the definitive histopathological examination have high sensitivity and solid specificity (Fig. 1).

For TIRADS 4, the IFS has a sensitivity rate of 58.3% and a specificity rate of 95.4% (Fig. 2), while for TIRADS 5, the IFS exhibits a sensitivity rate of 83.3% and a specificity rate of 100% (Fig. 3).

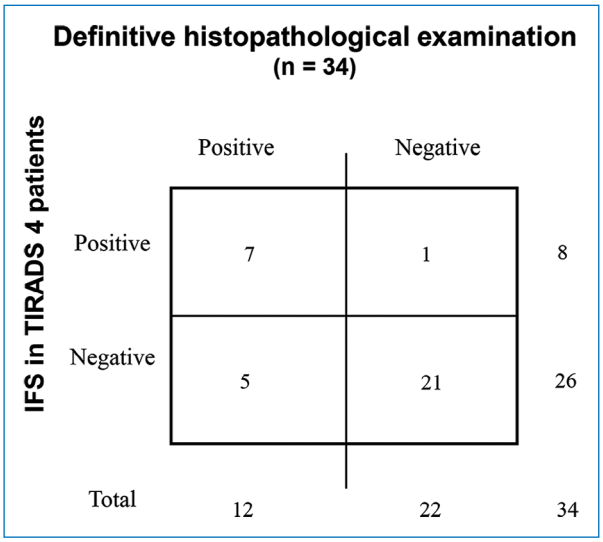

Figure 2. Sensitivity and specificity of intraoperative frozen section use in thyroid imaging reporting and data system four patients versus the definitive histopathological examination. Sensitivity: 58.3%; specificity: 95.4%; positive predictive value: 87.5%; negative predictive value: 80.7%; and accuracy: 82.3%.

Discussion

Thyroid IFS aims to determine which patients present malignant disease intraoperatively, which has an impact on the surgeon's decision-making regarding performing a more radical surgical technique.

The significance of assessing sensitivity and specificity lies in understanding the utility of IFS compared to the diagnostic standard and distinguishing patients who require more aggressive treatment from those who do not, thus enabling the planning of an optimal approach that limits complications and unnecessary surgeries.

Numerous studies demonstrate very high specificity rates (94%, 75%, and 92%) and considerable sensitivity rates (73%, 94%, and 100%)[14]. Some more recent

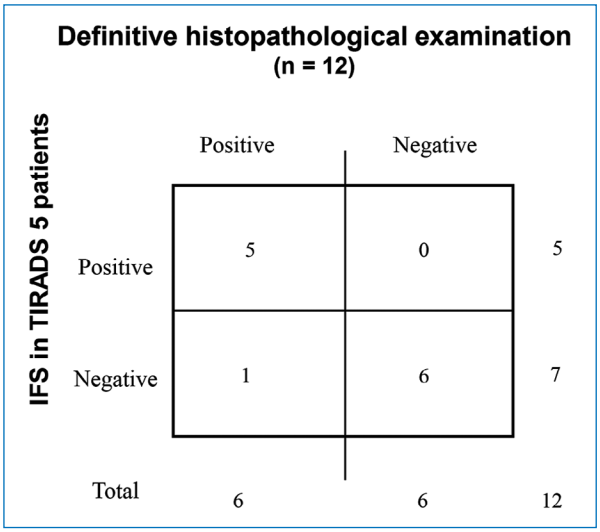

Figure 3. Sensitivity and specificity of intraoperative frozen section use in thyroid imaging reporting and data system five patients versus the definitive histopathological examination. Sensitivity: 83.3%; specificity: 100%; positive predictive value: 100%; negative predictive value: 85.7%; and accuracy: 91.6%.

studies report similar figures: A sensitivity rate of IFS in benign diagnosis of 94%, a specificity rate of 93%, and efficacy rates of 93.5%[17]. The results obtained in this study in the overall population are similar to those cited in the global literature.

This study confirms the intrinsic relationship between thyroid cancer and the female versus male sex (8.2:1), which is consistent with the current scientific medical literature available[2,3].

In this study, there is a predominance of benign outcomes 3 times greater in TIRADS 4 with respect to positive results for malignancy, while in TIRADS 5, there is a similar ratio of benign and malignant cases. However, this could be due to the fact that, when performing frozen section and multi-cut IFS, some segments may present malignancy; that is, a histological section could not be representative of the entire surgical specimen[17,18].

For patients with benign IFS and malignant IFS with tumor-free margins, it was not deem necessary to change the surgical approach by expanding the direction or performing radical thyroidectomy.

There is dominance in the affected right side compared to the left one; yet, this varies depending on the consulted literature.

Euthyroid function is the most prevalent in the studied population. It shows that the nodules are hypocaptant and it is mentioned that this type of nodules has little relation to thyroid cancer[5]. However, in our population, despite the aforementioned, all had cancer, predominantly benign, nevertheless confirmed by definitive histopathological examination.

The main limitation of this study is the small, single-center studied population. More multicenter studies with a larger population are needed to compare the results obtained in this study.

The combined use of FNAB with IFS is recommended to increase diagnostic sensitivity and specificity[17,19]. It is advisable to compare the diagnostic sensitivity and specificity of FNAB alone and combined with IFS by stages and compare the outcomes with this study, thus providing a comprehensive overview toward an improved diagnosis in patients with thyroid nodules.

Conclusions

In patients with advanced-stage thyroid nodules (TIRADS 5), IFS has better sensitivity and specificity compared to other previous stages.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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