Simultaneous Fine Needle Aspiration Biopsy and Trucut Needle Biopsy for the Diagnosis of Thyroid Nodules: Concordance and Diagnostic Performance

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Summary

We retrospectively reviewed medical records of 71 patients who underwent simultaneous fine needle and core biopsy of the thyroid gland at the Fundacion Santa Fe de Bogota, during the period between 2003-2007. Citology and pathology samples were reviewed blindly by two independent observers (one cytopathologist and one pathologist). Low agreement was found between the two methods. Kappa statistic was 0.351 (0.22-0.249 CI95%). Diagnostic performance was similar for both methods. The number of inadequate samples was 0% when both methods were combined. Fine needle biopsy classified correctly 100% of the malignant lesions, 100% of the follicular lesions and 62% of the benign lesions when compared with surgical specimens.

Key words

Thyroid gland
Aspiración con aguja fina y biopsia con aguja trucut simultáneas para el diagnóstico de nódulos tiroideos: concordancia y rendimiento diagnóstico

Resumen

**Objetivos:** Establecer la concordancia entre la biopsia mediante aspiración con aguja fina y la biopsia con aguja TRUCUT 20G para el diagnóstico de nódulos tiroideos en pacientes remitidos para biopsia en la Fundación Santa Fe de Bogotá; determinar el rendimiento diagnóstico de cada uno de estos métodos de forma independiente y combinada, y establecer el porcentaje de complicaciones asociadas al procedimiento.

**Método:** Se revisaron de forma retrospectiva los registros de 71 pacientes con biopsias simultáneas de tiroides con aguja fina y aguja TRUCUT durante el período 2003-2007. Un patólogo y un citopatólogo analizaron de forma ciega e independiente las muestras de citología y de tejido que se habían obtenido y así clasificaron a los pacientes en: tejido tiroideo normal, lesiones benignas, anormal, lesiones de células foliculares y neoplasias malignas. **Resultados:** La concordancia entre la biopsia con aguja fina y la biopsia con aguja TRUCUT 20G fue baja. Cuando se compararon los reportes de patología y citología con los del especímen quirúrgico, se encontró un mayor porcentaje de acuerdo en las biopsias con aguja fina, que clasificó correctamente 100% de los carcinomas, 100% de las lesiones de células foliculares y 62% de las lesiones benignas. **Conclusiones:** La concordancia entre la biopsia con aguja fina y con aguja TRUCUT es baja, por lo que no son intercambiables estos dos métodos diagnósticos. Aunque el
Thyroid nodules are a frequent condition. Their prevalence is 4-7%, with an incidence of less than 50 per million inhabitants (1). The probability of malignancy in a thyroid nodule is affected by several factors: it is more frequent in patients under 20 years of age and over 60 years of age, and increases in patients with nodules that are firm on physical examination, have rapid growth, are attached to the deep tissue layers of the neck, and are associated with vocal chord paralysis or regional adenomegalies. Furthermore, a history of neck irradiation or thyroid cancer in the family also increases the risk of malignancy in a thyroid nodule.

In comparison with the high incidence of thyroid nodules in the adult population, the prevalence of cancer is low (2). Only 5-15% of surgically resected thyroid nodules are malignant (3).

Most thyroid carcinomas are papillary carcinomas (75-80%). Other types of thyroid carcinomas include follicular carcinomas (10-20%), medullar carcinomas (5%) and anaplastic carcinomas (1-2%). Although thyroid cancer morbimortality is low compared with other carcinomas. The calculated survival for papillary carcinoma is 95% at 30 years; morbimortality increases in older patients and in those with more
advanced stages of the disease at the time of diagnosis (4). Therefore, early diagnosis is of critical importance.

Evaluation of a thyroid nodule usually begins by an imaging study, whether it was initially discovered by palpation on physical examination or incidentally when performing an imaging study of the neck.

Neck ultrasound is currently the diagnostic method of choice to assess the thyroid gland. In the first place, it is important to know the definition of thyroid nodule. For practical purposes, a thyroid nodule is a lesion distinguishable from the rest of the thyroid tissue by US. Echographically, there are several criteria that have been taken into account in the evaluation of thyroid nodules, with the purpose of differentiating benign from malignant nodules. These include size, echogenicity (hypoechoic, isoechoic, hyperechoic), composition (solid, cystic mixed), the presence of calcifications (microcalcifications or gross calcifications), and the determination of flow characteristics by means of color Doppler (peripheral or internal). Many studies published in the literature have tried, based on these ultrasound characteristics, to predict the probability of benignity or malignancy of a thyroid nodule (2,4).

In general terms, it has been found that nodule size is not a predictor of malignancy, since the probability of a carcinoma is the same for large and small nodules. However, there are other characteristics that have been shown to have a greater association with the risk of cancer, among them, the presence of microcalcifications, nodule hypoechogenicity, irregular borders predominantly solid composition, and internal vascularization as seen on Doppler color images. Although operative characteristics for each of the criteria reported in the literature have been extremely variable between all the studies, none of them have been shown to have high sensitivity or specificity for US diagnosis of thyroid cancer.
The characteristic with greatest sensitivity (69-75%) is the solid composition of the nodule, which has a very low positive predictive value, between 15-27% probability of malignancy. On the other hand, the presence of microcalcifications is the echographic characteristic that has been shown to have the greatest positive predictive value, between 41-94%. However, microcalcifications are only found in 26-59% of thyroid carcinomas, which implies low sensitivity. For all these reasons, it has been considered that the combination of all the echographic criteria improves the positive predictive value in the diagnosis of cancer (2).

The use of color Doppler alone cannot be considered a reliable method to determine whether a nodule is benign or malignant. Some studies have reported that the central flow in a nodule is visualized more frequently in malignant nodules than in benign ones (42% in comparison with 14%)(5).

Given the variability of the positive predictive value of the echographic characteristics described for thyroid nodules, it is not possible to take a patient to surgery based only on an image. It is necessary to have a histological diagnosis prior to surgery, so that those patients with thyroid cancer can have an early diagnosis and receive timely treatment so as to reduce to a minimum the morbimortality of this disease, while at the same time avoiding unnecessary exams and operations in patients with benign nodules.

Therefore with the aim of unifying criteria to determine which thyroid nodules will require a histological diagnosis, the Society of Ultrasound Radiologists published, in October 2005, a consensus document for the management of thyroid nodules.

Biopsy is recommended in solitary nodules ≥ 1cm in greater diameter, that have associated microcalcifications, and in those ≥ 1.5 cm in greater diameter, that are solid, predominantly solid, or present gross calcification. Nodules > 2 cm in greater diameter
must be biopsied if they have a mixed composition, cystic and solid, or a solid wall component or if the nodule has grown significantly since the last study. Biopsies are not considered necessary in patients that have predominantly cystic nodules that do not have any of the other characteristics described. In patients with thyroid gland multinodular disease, it is advisable to perform biopsies on those nodules that have the characteristics described above.

If a patient presents regional adenopathies in the neck, a biopsy must be performed, and a sample taken from one of the abnormal lymph nodes or from an ipsilateral thyroid nodule. This is because in some patients, lymph node metastasis of a papillary carcinoma that is still not visible on US, may appear first. The abnormal characteristics of these lymph nodes that are associated with a greater risk of cancer include: heterogeneous texture, presence of calcifications, cystic areas within the lymph node and loss of oval morphology, or its fatty hilum. The probability of malignancy increases with node size: lymph nodes with a short axis diameter > 7 mm must be considered suspicious for malignancy, and must be biopsied (2).

Keeping these criteria in mind, diagnosis by means of biopsies is considered an integral part of the evaluation of patients with thyroid nodules with suspicion for malignancy. Percutaneous thyroid biopsy is easy to perform, has a low cost, and with adequate tissue samples taken with US guidance, has improved diagnostic certainty in this type of condition. Currently, this is done with 2 types of needles, fine needles (FNB) or cutting needles (TRUCUT).

Fine needle biopsy (FNB) has become the initial diagnostic exam in most patients with thyroid nodules, since it is a minimally invasive method, safe, economic and is done in an outpatient. In the literature, different sensitivities and specificities have been reported for FNB. Sensitivity varies from 65-98%, and specificity from 52-100%, with
positive predictive values from 46-100% and negative predictive values from 83-95% (6). With echographic guidance the operative characteristics of FNB improve, and sensitivities and specificities of 100% have been reported (6). This variability between studies reported in the literature is due, in great part, to the fact that this technique not only depends on operator experience, but also, on the cytopathologist who analyzes the sample. In skilled hands, the degree of confidence for this technique is calculated to be between 95-98%, for false negatives and false positives between 1-3% (6).

Cytological specimens are classified, typically, in four categories: negative (benign), positive (diagnosis of cancer), suspicious for malignancy or follicular neoplasm, and non-diagnostic. Of the FNBs classified as suspicious for malignancy, 30-65% will correspond to carcinomas seen in the surgical specimen. “Non-diagnostic” samples are those that contain a lower number of cells than those required for a histological diagnosis, and those have been reported to be between 15-20% of samples even in centers with wide experience. This is, therefore, one of the main limitations of this technique. This becomes a very important fact if you consider that 5-9% of patients with non-diagnostic samples end up with a diagnosis of cancer (7,8).

Core biopsies with TRUCUT needles contribute a greater volume of tissue, and furthermore maintain its cellular architecture, which makes it possible to be more precise when making a histological diagnosis. However, this method has not been widely used, because a greater risk of associated complications has been perceived. Another limitation is that, since one or two cylinders of tissue can be obtained, given the greater caliber of the needles currently used (14-18 G), there is a greater probability of error when taking the sample (1).

At the Radiology Department of Fundación Santa Fe de Bogota, thyroid percutaneous biopsy with TRUCUT 20G needles was implemented several years ago
for the diagnosis of thyroid nodules, with a low percentage of associated complications. Patients tolerate the procedure very well and the Pathology Department has supported the use of this method due to the quality of the samples obtained, which has allowed them to improve their diagnostic performance for this condition.

The objective aim of this study is to measure the concordance between both procedures in the same population, so that the results allow us to choose the best diagnostic strategy for patients with thyroid nodules, and to extrapolate this to other institutions in Colombia.

**Materials and Methods**

The data base of thyroid biopsies of the Department of Diagnostic Images of the Fundación Santa Fe de Bogotá was reviewed and the registers of 115 patients who had undergone simultaneously ultrasound guided percutaneous thyroid FNB and core biopsy with TRUCUT were obtained. Of these biopsies we were only able to obtain sections and tissue samples of 71 patients who complied with the following inclusion criteria: patients referred to the Department of Diagnostic Images of the Fundación Santa Fe de Bogotá between 2003 and 2007 for percutaneous biopsy of thyroid nodules; that had undergone simultaneous FNB and core biopsies with TRUCUT 20G needles, and patients for whom it was possible to obtain, from thyroid US reports or directly from the image archives, information on the nodule biopsied (location, size, echogenicity, composition, presence of calcifications and flow pattern). Exclusion criteria were: history of partial or total thyroidectomy with biopsy of thyroid tissue suspected of relapse, patients sent for a second biopsy due to insufficient or abnormal sample according to pathological criteria, and patients with cytological sections and tissue
samples not available at the Pathology Department for a blind analysis of both samples by a cytologist (AS) and a pathologist (AG).

All patients underwent a careful physical exam and, prior to biopsy taking, an US of the thyroid gland, with Doppler analysis to characterize the thyroid nodule to be biopsied. Informed consent was obtained to perform the biopsy in all patients, according to the regulations of the institution. The biopsies were performed by three radiologists with more than 10 years' experience in ultrasound guided procedures.

Patients were placed in a supine position on the gurney with a rolled up pillow placed under the cervical region to extend the neck. Toshiba Aplio equipment was used in most cases, with high resolution 7.5-12 Mhz linear transducers, which were used to guide the biopsy. After aseptic and antiseptic procedures the skin was infiltrated with local anesthetic (lydocaine 2%) at the chosen site.

By means of a coaxial system with a yelco 14G jacket, the needles were advanced to take the biopsies. The FNB were always performed first and, subsequently, the same number of samples were taken with the TRUCUT needles. In general, from 3 to 4 samples were taken with each needle, but the same number of samples were always taken with both.

The aspirated material was extended on a previously marked slide, fixated with ethyl alcohol 95% and sent to the Pathology Department for its interpretation. The tissue cylinders were laced immediately in a 10% formaldehyde solution for subsequent processing. The puncture site was compressed and the soft tissue of the neck was assessed to rule out possible complications.

In the Pathology Department the samples were analyzed independently by an expert cytopathologist (AS) and by a pathologist who also had a wide experience with thyroid studies (AG), they had to register on a form if the biopsy was a FNB or a
TRUCUT core biopsy, if the sample was sufficient or insufficient, and the diagnostic category of the sample.

Results

A total of 71 patients were included in the study, between 2003-2007, that complied with the inclusion criteria. The patients had an age range of 15-81 years, with a mean age of 47.5 years and a median age of 48 years. And 57 (80.2%) were women and 14 (19.7%) were men (Table 1).

Table 1. Demographic Characteristics of the Population of the Study

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age (years)</td>
<td>71</td>
<td>100</td>
</tr>
<tr>
<td>Mean (standard deviation)</td>
<td>47.5 (14.8)</td>
<td></td>
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<tr>
<td></td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>15-81</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
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<tr>
<td>Masculine</td>
<td>14</td>
<td>19.72</td>
</tr>
<tr>
<td>Feminine</td>
<td>57</td>
<td>80.28</td>
</tr>
</tbody>
</table>

A total of 71 nodules were biopsied, the majority were located in the right lobe of the thyroid gland (Fig.1), with greater diameters of 4-53 mm (mean 19.8 mm). These were predominantly hypoechoic, in 47.8% of cases; predominantly anechoic, in 23.9% of cases; with equal distribution between nodules, predominantly isoechoic or
hyperechogenic (14.08%) (Fig.2). Of solid composition 49.3% of cases and mixed, 50.7% (Fig.3). As to the presence of calcifications, 57.75% had no associated calcifications, whereas 32.39% had microcalcifications and 9.86% had gross calcifications (Fig. 4). With a certain relative frequency the information on nodule flow pattern was lacking in the reports of the biopsies and US procedures (31% of cases). When it was reported, it was peripheral to the nodule in 26.76% of cases; central in 29.58% and there was no flow in 12% (Fig. 5).

In the cytology reports of the FNB, the most frequent diagnosis was goiter, followed by follicular lesions (probably adenomatous goiter) and papillary carcinoma (Fig. 6). In the pathology reports, the most frequent diagnosis was, as in the cytology reports, goiter; followed by follicular cell lesions (probably adenomatous goiter), with a frequency equal to that of papillary carcinoma of the thyroid (Fig. 7).

When a diagnostic cumulative study was performed, according to the 5 major categories and the histological classification of the lesions in the thyroid gland, a greater percentage of diagnoses of benign lesions was found with both types of needles, followed by follicular cell lesions and malignant neoplasms, in second and third place, respectively.

Malignant neoplasms were more frequently diagnosed by cytology (FNB), whereas pathological studies (TRUCUT core biopsies) reported a greater percentage of benign lesions (Fig. 8). The concordance between both biopsy methods, determined by a weighted kappa, according to the investigator, was calculated in 0.3521 (0.22-0.49 CI 95%) with linear weights it was calculated at 0.2821 (0.12-0.45 CI 95%) and with quadratic weights it was calculated at 0.2635 (0.03-0.49 CI 95%).

Of the total of histopathological diagnoses of 71 nodules, the percentage of samples in which both diagnostic methods totally agreed was 50.7%. With reference to
the cytological reports of benign samples, (FNB), pathology studies (core biopsies with TRUCUT needles) agreed with 75% of the samples, whereas for malignant reports they agreed with 57.3%. Of the pathology reports of benign samples, (core biopsies with TRUCUT needles), cytology studies (FNB) agreed with 54.8% of the samples, whereas for malignant reports they agreed with 100%.

Of the 71 nodules biopsied, 20 (28%) underwent surgery at the Fundación Santa Fe de Bogotá, and the reports of the surgical specimens were obtained, so it was possible to compare the cytology and pathology reports independently. Of the 20 surgical specimens (8 corresponded to benign pathology reports [goiter and thyroiditis], 10 to malignant conditions (papillary carcinoma) and 2 to follicular cell lesions (Fig. 9).

The cytology and pathology reports were compared independently with the surgical specimen reports and it was found that cytology agreed in 100% of cases with malignant pathologies (papillary carcinoma) and 100% of follicular lesions; whereas in the case of benign lesions the cytology reports agreed with 62% of the cases. Follicular lesions were the condition that generated most confusion, since 37.5% of the cases on which there was no agreement were reported as follicular lesions. Pathology reports (core biopsies with TRUCUT needles) agreed with 50% of the benign reports, 50% of the follicular cell lesions and 60% of the papillary carcinoma reports obtained from the surgical specimens.

A proportional comparison was made to detect if there were differences in the amount of sufficient sample according to the type of needle used: 8.45% (6/71) FNB samples were insufficient and 9.86% (7/71) TRUCUT samples were insufficient. No statistically significant differences were found between both biopsy methods (p>0.99). When both methods were used in a combined manner, the number of insufficient
samples decreased to zero (0). The percentage of complications decreased (2.8%), and these were only hematomas, which were small and managed with local treatment.

**Discussion**

Diagnostic images, especially ultrasound, are currently the most important tool for the diagnosis of thyroid nodules, a condition with a high incidence in our practice.

Unification of ultrasonographic criteria to obtain a better characterization of thyroid nodules has made it possible to biopsy fewer patients and, ultimately, perform surgery on fewer patients, thus increasing the incidence of malignancy in surgical specimens. Our results agree with those of studies published in the literature, since most nodules biopsied showed characteristics that, when present, according to the consensus guidelines for thyroid biopsy, are an indication for biopsy. These include nodule hypoechogenicity (47.8%), solid or mixed composition (49.3% and 50%, respectively), the presence of microcalcification (32.39%) and flow within the nodule (29.58%).

Similarly to other studies published in the literature (9, 10, 11), follicular cell lesions were, also, the condition most difficult to diagnose, since they were part of non-concordant diagnoses in most cases, both for FNB biopsies and TRUCUT biopsies.

Since the concordance between both diagnostic methods was low, which means that the methods are not interchangeable, and keeping in mind that when comparing reports obtained by each method with the surgical specimen reports (only in 28% of the patients), FNB showed greater concordance. If one method had to be chosen based on effectiveness to detect malignant lesions, FNB should be chosen. This agrees with several studies reported in the literature, among them the one published by Dr. John Boey (9), in which greater diagnostic performance was reported for FNB than for TRUCUT needle biopsies (93% in comparison with 52%). The lower diagnostic
performance of core biopsies with TRUCUT needles could be explained by greater
technical difficulties, especially for obtaining samples from lesions located medially in
the thyroid gland and small lesions.

Insufficient samples were 8.4% for FNB and 9.8% for core biopsy with
TRUCUT, with no statistically significant differences between both methods. However,
when the combination of both biopsy methods was considered, diagnostic performance
increased to 100%. These data agree with the study published by Dr. Steen Karstrup, in
which no statistically significant differences were found in the diagnostic performance
of each method (97% for FNB and 88% for TRUCUT), but when they were combined,
this increased to 100% (12).

One of the limitations of our study was the loss of 44 patients, for whom no
samples were found in the Pathology Department, since their inclusion in the study
could have improved the precision of the results. The correlation of only 28% of the
samples obtained with the corresponding surgical specimen could have affected the
validity of the results.

Another limiting factor was the lack of standardization of the sample taking
technique. As this was a retrospective study, it was not possible to unify criteria for
sample taking. For other studies comparing these two diagnostic methods, it is
indispensable to always take the same number of samples with both needles, and also to
randomize the first sample taking.

Since in this study only concordance and diagnostic performance of FNB and core
biopsies with TRUCUT needles were evaluated, it is necessary to keep in mind that
other variables are important, before thinking of changing the diagnostic strategy
currently in use at the Fundación Santa Fe de Bogotá. For example, a cost study and a
patient satisfaction study using both methods simultaneously, or only one, but with the possibility of carrying out a re-biopsy if the sample is insufficient.

Conclusions

The concordance between FNB and TRUCUT 20G needle biopsies is low, which means these 2 procedures are not interchangeable. FNB had better concordance with surgical specimens than TRUCUT biopsies. There was no statistically significant difference in the percentage of insufficient samples between FNB and TRUCUT biopsies, however, when these were combined, the diagnostic performance of thyroid percutaneous biopsies increased to 100%. To determine which is the best diagnostic strategy in patients with thyroid nodules, it is necessary to perform additional studies of costs and patient satisfaction.

References


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Figures

![Pie chart showing distribution of nodules in the thyroid gland.](image)

*Fig. 1. Localización del nódulo de acuerdo con la distribución anatómica de la glándula tiroides*

Right  Left  Isthmus

*Fig. 1. Location of the nodule according to the anatomy of the thyroid gland*
Fig. 2. Frequency distribution according to nodule echogenicity

Percentage

Anechoic   Hypoechoic   Isoechoic   Hyperechoic

*Fig. 2. Frequency distribution according to nodule echogenicity*
Fig. 3. Frequency distribution according to nodule composition: cyst, solid and mixed

Solid  Mixed
Fig. 4. Frequency distribution according to associated calcifications

Gross  Micro  No calcifications

Fig. 4. Frequency distribution according to associated calcifications
Percentage
Peripheral    Internal    Without    Not reported

*Fig. 5. Frequency distribution according to the flow pattern observed with color Doppler*
Fig. 6. Distribution of diagnostic categories for the classification of thyroid gland lesions in the cytology reports

Percentage

Goiter  Thyroiditis  Cysts  Suspected malignity  Indeterminate (adenomatous goiter vs)  Probably adenomatous goiter  Probably follicular neoplasia  No Dx.

Fig. 6. Distribución de los reportes de citología entre las categorías diagnósticas de la Clasificación de lesiones de la glándula tiroides
Fig. 7. Distribution of diagnostic categories for the classification of thyroid gland lesions in the pathology reports

Percentage

Goiter Thyroiditis Cysts Suspected malignity Indeterminate (adenomatous goiter vs) Probably adenomatous goiter Probably follicular neoplasia No Dx.
Fig. 8. Comparative distribution of the frequencies of the 5 main categories according to the classification of lesions of the thyroid gland in the cytology and pathology reports.

Percentage

Cytology  Pathology

No Dx Abnormal

Malignant neoplasias Benign lesions

Adenomatous follicular cell lesions
Fig. 9. Frequency distribution according to the reports of the surgical specimens of the patients operated at the FSFB

Percentage

Goiter Thyroiditis Probably follicular neoplasia Papillar carcinoma

Fig. 9. Distribución de frecuencias de acuerdo a los reportes de los especímenes quirúrgicos de pacientes intervenidos quirúrgicamente en la FSFB