



## Diagnostic Generalities of Thyroid Cancer

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### Abstract

Scientific-technical advances have made it possible to specify that thyroid cancer is the most common malignancy of the endocrine system, with more annual deaths compared to other cancers of endocrine origin combined; despite the low mortality rate. Thyroid Cancer is a malignant tumor or growth caused by the abnormal and uncontrolled development of cells that invade and destroy thyroid tissue, currently being the most frequent endocrine neoplasm. A bibliographic review of the selected topic was carried out, at the same time the Infomed platform was considered on its Scielo consultation site of Cuban and foreign authors, in addition to the Internet, the consultation library of the Dr. Juan Bruno Zayas Alfonso General Hospital. A total of 36 bibliographic from various authors were analyzed; which allowed the analysis and discussion of the results obtained, in a comparative manner according to the sections. We proceeded to assess and give an opinion about this disease, taking into account an ethical and professional framework. It is concluded that it is important to know the clinical and diagnostic generalities of thyroid cancer in the current context because health professionals must appropriate the clinical and epidemiological method to know the classification of this disease, the type of cancer, the anatomopathological variety, the presence or absence of metastases, which reveals the need to indicate, perform and interpret complementary tests, depending on the scientific and technical availability of each laboratory. This aspect is widely debated by multidisciplinary groups that deal with thyroid cancer, an alert is being carried out worldwide to work on the risk factors of this neoplasm to reduce incidence, prevalence and mortality..

### Background

Serious forms of thyroid cancer have been defined since ancient times, with surgical treatment being described in the Ebers papyrus. Galen described this gland for the first time in 1656, and in 1776 Albrecht von Haller described the thyroid as a gland without a duct and attributed several imaginative functions, including the lubrication of the larynx, a blood reservoir for the brain and that of an aesthetic organ to enhance the beauty of the female neck, for his part [1,2]. Initially, the thyroid was recognized as an important organ when it was observed that its enlargement was closely related to a series of changes that affected, mainly the eyes and the heart, which were later related to hyperthyroidism.

Thyroid Cancer is a malignant tumor or growth caused by the abnormal and uncontrolled development of cells that invade and destroy thyroid tissue, currently being the most frequent endocrine neoplasm. The first account of a thyroid operation was in 1170 by Roger Frugardi, was considered a dangerous procedure with high mortality rates, often confusing primitive cancer with secondary cancer [2,3].

Evolutionarily for the middle of the 19th century, advances appeared in anesthesia, antisepsis and in the control of homeostasis, which allowed surgeons to operate on the thyroid with the consequent reduction in mortality. In the year 1811 Rolleston described the thyroid carcinoma, in 1822, Chetuis discovered a precise description of the glandular histology and pointed out the hardness, dyspnea, pain and invasion of the neighboring structures.

During this period Theodore Kocher described a clinical study on malignant tumors of this gland and verified the appearance of myxedema and tetany after a thyroidectomy. For this reason, he was considered a pioneer of thyroid surgery at the beginning of the 20th century. He also proposed subtotal thyroidectomy to avoid these complications, and was also known as the founder of the conservative surgery of this gland. Despite the scientific arguments, during this time the need for surgical treatment was noted; supported not only by clinical criteria, but also by histological, cytological and pathological aspects.

Ultimately, in the year 2000, the medical colleges specified the significance of the invasion of blood

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vessels in thyroid cancer and showed the biological, histological and response to treatment behavior. Important research on thyroid cancer, specifically diagnosis and therapeutics, has recently been described. Means, Lahey, Rienhoff Revealed the origin of cancer in the thyroid gland, described metastases and differentiated primary from secondary cancer.

Scientific-technical advances have made it possible to specify that thyroid cancer is the most common malignancy of the endocrine system, with more annual deaths compared to other cancers of endocrine origin combined; despite the low mortality rate. Numerous medical investigations describe the increase in patients with Thyroid cancer caused by some environmental cause, either due to increased exposure to radiation or some other toxic exposure. Duffy and Fitzgerald reported the appearance of papillary thyroid carcinomas and their relationship with radiation exposure, mainly in children with history of having received therapeutic radiation to the head or neck during infancy or childhood, due to adenotonsillar or thymic hypertrophy [5-7].

In 2015, it was found in one of the US states that approximately 67% of thyroid cancer diagnoses occurred in people under 55 years of age and approximately 2% of those diagnosed occurred in children and young people. The American Cancer Society in 2016 described about 64,300 new cases of thyroid cancer, of which 49,350 cases would occur in women and 14,950 in men [8,9].

In the United States, thyroid cancer accounts for 4% of all newly diagnosed neoplasms with approximately 13.5 new cases per 100,000 population. The survival rate has been estimated at 97.9% at 5 years with low mortality, calculated at approximately 0.5 per 100,000 people/year. In Spain, other European and Asian countries, the rates show similar results [10]. Developed countries publish that this disease affects women more frequently, with an approximate ratio of 3 to 1. In Colombia, the adjusted incidence rate for the period between 2007 and 2011 was 1.1 per 100,000 men and 9.7 per 100,000 women occupying the tenth place in frequency.

Mexico reported 3,195 cases of thyroid cancer (1,351 in men and 1,844 in women), which represented 2.5% of all malignant neoplasms, with an incidence of 3 per 100,000 inhabitants and a mortality of 0.6 per 100,000 inhabitants [11,12]. The American Cancer Society estimated 56,870 new cases of thyroid cancer in 2017, with approximately 2,010 deaths among the estimated 350,000 patients with the disease in the US.

In the United States estimates that: About 52,070 new cases of this disease will be diagnosed (14,260 in men and 37,810 in women). About 2,170 people will die from this cancer (1,020 men and 1,150 women). Emphasizing that it is increasing most rapidly in the United States, and has tripled in the past three decades, due to the increased use of thyroid ultrasound that can detect small thyroid nodules that might not otherwise be found (thyroid incidentaloma) [13,14].

In Cuba it is transcendental that malignant tumors occupy the second place of cause of death, preceded by Cardiovascular diseases; together with this, the incidence rate of Thyroid Cancer ranges between 0.36 to 0.39 per 10,000 inhabitants, a study carried out in the City of Havana revealed that of 183 cases, 81.3% belonged to the female sex and the average calculated age was  $45.9 \pm 17.5$  years, Villa Clara and Matanzas presented equivalent results. In Cienfuegos, the incidence rates have been increasing in the last 5 years, the highest was detected in 2013 with 23 new cases and a rate of 5.7 per 100,000 inhabitants. In Santiago de Cuba, thyroid cancer is commonly diagnosed at a younger age compared to most other cancers that affect adults. In studies carried out at Hospital General "Dr. Juan Bruno Zayas Alfonso" of Santiago de Cuba in the year 2013, the prevalence of patients aged 31-45 years and the female sex (38, for 45.2%), with an average age of 40.9 years, was demonstrated [15-17].

It is necessary to reflect on the theme that is addressed since; In recent years, the diagnostic frequency of this thyroid pathology has increased and it constitutes one of the entities with the highest attendance at surgery consultations; An increased incidence of this cancer has been reported, especially due to papillary carcinoma, which represents 49.0% of all thyroid cancers in nodules  $\leq 1$  cm and 87.0%, as well as in those  $\leq 2$  cm in diameter [18].

Currently, an increase in the incidence and prevalence of thyroid cancer has been observed. Therefore, a perennial scientific-technical development is required, which allows the incorporation into the performance of the health professional, clinical judgments, methods, skills, algorithms, strategies that allow specialists in Surgery to investigate and go through the most innovative definitive treatment of this neoplasm. It is a necessity for these professionals to update aspects with a level of recognized scientific evidence. The objective of this bibliographic review is to describe the novel aspects related to the clinical and therapeutic diagnosis of Thyroid Cancer [19].

**Scientific problem:** What would be the novel aspects from the clinical and diagnostic point of view about Thyroid Cancer today?

## Developing

The clinical and diagnostic generalities of thyroid cancer directly reflect the classification of this disease, the type of cancer, anatomopathological variety, the presence or absence of metastasis and the procedures of the clinical method applied by professionals who have developed sufficient competence to comprehensively address this pathology. Consequently, in the diagnosis of this disease, the questioning is of vital importance because it suggests and guides the exhaustive physical examination; it must be carried out effectively, in conditions of privacy for the patient, since it expresses 80% of the diagnosis [19,20].

The analytical determination of Thyroid Cancer requires knowledge of the risk factors, the symptoms and the final result of the complementary tests; which responds to the diagnosis of the disease and affects the selection of the appropriate treatment and the increase in quality of life. Despite the fact that this cancer is currently the most frequent endocrine neoplasm, of all malignant endocrine tumors (90%), it represents, on a global scale, more than 1% of all neoplasms, including cutaneous ones.

Being more frequent in women between 25 and 65 years of age; It is pointed out that the incidence of thyroid cancer is approximately 9/100,000 per year and increases with age. It is uncommon before the age of 20 and comprises only 1% of all malignant tumors that occur before the age of 18, with an excellent prognosis, unlike when it appears after the age of 65. In 2008, it was estimated that in the United States more than 37,000 adults would suffer from thyroid cancer and 1,600 of them would die from this cause, with a progressive increase in its incidence [21,22].

From the clinical point of view, currently in Cuba there has been an increase in the incidence of thyroid cancer, for several consecutive years it represents one of the ten most frequent neoplasms in the female sex with a gross rate of 8 x 100,000 inhabitants. Mortality due to this disease is low and ranges between 0.36 and 0.39.

In the province of Pinar del Río, in correspondence with the above, the numbers of diagnosed cases have been increasing in recent years [2]. Jiménez García Y et al. With the investigation: Characterization of patients with thyroid pathologies who underwent surgery at the Abel Santamaría Cuadrado General Teaching Hospital, they found that 38.46% of the cases had thyroid cancer. Other studies related to the anatomy of the thyroid gland in Cuba showed that nodular thyroid disease occurred more frequently at the lobular level, predominantly on the left, findings that agree with those found by Pérez González OF

et al. [6]. In a study carried out in the province of Las Tunas, when evaluating the location according to the degree of malignancy of the lesions, a greater number of patients with right lobe involvement was shown for benign lesions and the opposite for malignant lesions [28]. Reyes Dominguez Y et al. in Guantánamo province, they revealed that the malignant nodule was located more frequently in the left lobe [1-4].

An investigation of 30 patients with differentiated thyroid cancer, who received oncospecific treatment at the Conrado Benítez García Oncology Hospital in Santiago de Cuba, between January 2014 and July 2017; projected that 46.7% could not specify the presence of a risk factor. Regarding the clinical manifestations at the time of the initial consultation, the most frequent was the increase in the volume of the gland in 26 patients (86.7%). To a lesser extent, other symptoms appeared [1].

The authors considered that clinical findings evidenced in national investigations demonstrate the individualized diagnostic accuracy of these patients, the need to identify risk factors as well as the correct examination of the thyroid gland accompanied by propaedeutic maneuvers that enrich semiological precision for early diagnosis of thyroid cancer.

### Related to complementary exams

The diagnosis of patients with thyroid cancer is a clinical, instrumental, imaging and pathological challenge, and although it does not represent a health problem in Cuba, its very complex and its conduct has a multidisciplinary approach, there are clinical-epidemiological, imaging and histological elements to diagnose thyroid cancer [3,4].

It should be noted that since the laboratory emerged, it has provided results that are integrated into the clinical method since the complementary ones have a role that is not only important, but sometimes decisive in the diagnostic process. Therefore, the patient will be evaluated from the humoral point of view, which includes:

Hemogram shows that there is always a degree of anemia, although red blood cells rarely fall below 3,500,000 with anisocytosis, poikilocytosis and polychromatophilia.

White blood cells can rise to 10 or 12,000 and this moderate leukocytosis is constant, falling on polynuclear neutrophils.

Determination of thyroid-stimulating hormone (TSH) and free sodium levothyroxine: 3, 5,3',5'-tetraiodo-L-tyronine (thyroxine, T4) by the laboratory [23,24].

The determination of the levels of thyroid hormone, allows to evaluate the function of the gland and to be able to identify patients with hyperthyroidism and subclinical hypothyroidism. In addition, if it is elevated, it allows cytological evolution (probability of malignancy), for which it is of vital importance for the therapeutic to impose.

Serum thyroglobulin (Tg): Elevated in most thyroid diseases, it is neither sensitive nor specific on CT [25].

Serum calcitonin: It can detect C-cell hyperplasia and micromedullary carcinomas of the thyroid of questionable clinical significance. If levels of serum calcitonin not stimulated with pentagastrin > 100 pg/ml suggest the presence of medullary thyroid cancer.

Tumor markers that are genetic tests that are often used to guide cancer treatment, but have a high cost, so their use is left for cases of difficult diagnosis: o Carcinoembryonic antigen (CEA), or BRAF or RAS

Genetic testing and refinement of oncogenes is an area of ongoing active research. Greater knowledge of this area will improve the way treatment options are chosen and give a more accurate prognosis.

Thyroid FNA, which was developed by Sodestron, in Stockholm, Sweden, in the 1950s [25-27].

In Cuba, it was used systematically in the second half of the 1980s and can be considered as a diagnostic technique or good selection of patients who are candidates for surgical treatment, being able to reduce with it the number of thyroidectomies in the case of benign lesions. The causes of "mistakes" in the diagnosis of HFNC once the diagnosis of the injury has been established may be due to both the nature of the injury and errors in interpretation.

The same was described in a study carried out in the General Surgery Service of the "Saturnino Lora Torres" Provincial Teaching Hospital in Santiago de Cuba during the five-year period 2007-2011, applied to 204 patients operated on and discharged for nodular thyroid diseases [1-4].

CAAF was not sensitive, considering that 20 patients (9.8%) with thyroid carcinoma were not correctly diagnosed during the pre-surgical evaluation and, since the condition was considered benign, they underwent an initial conservative operation, so they were re-operated to complete the total thyroidectomy, once the final biopsy result was received by embedding in paraffin.

This shows that the results of the studies are not always reliable. Factors such as: performance error, sample contamination, lack of resources or instruments, or simply technical error, influence the aforementioned. We must apply the clinical method and carry out the greatest number of tests to make a diagnosis

The radiological study of the thyroid is very important; It shows the existence of a retro-sternal prolongation, allows us to appreciate the real dimensions of the tumor and its lower limit. Sometimes it indicates the presence of a mediastinal adenopathy, demonstrating the extension of the lymphatic invasion, which limits the possibilities of a radical intervention, or it shows a pulmonary generalization, or a pleural effusion.

Also, the X-ray can demonstrate tracheal deformations, since said air-filled conduit appears in contrast to the shadow of the neoplastic mass, indicating the existence of compression. Scintigraphy with Iodine (I 131) and other radioisotopes, which for decades played a fundamental role in the selection of patients for treatment, due to its low sensitivity and high cost, evaluating the structure and function of the thyroid gland, have been displaced and today they are only used in the follow-up and evaluation of patients operated on for well-differentiated thyroid carcinomas [28-30].

Ultrasound provides information on structural elements of the tumor, the gland and the cervical region. Related to the tumor, it evaluates the following elements: size, echorefringence, characteristics of the capsule, presence of calcifications and intratumoral circulation. Regarding the gland, it reports on its size, characteristics of its structure, especially the presence of other non-palpable nodules, especially in the contralateral lobe to the predominant nodule and in the cervical region, it can reveal adenomegalies not yet detected on physical examination in that area.

With the information collected, an assessment of the possible tumoral type of the lesion can be made, since there are elements of risk for malignant tumors, such as: solid, hypoechoic tumors, with a capsule that is not well defined and the presence of microcalcifications; It is also used in the follow-up of patients operated on for cancer and as a guide in percutaneous injection of ethanol and laser therapy.

Computerized Axial Tomography, Positron Emission Tomography and Nuclear Magnetic Resonance are used in tumors with symptoms and signs of infiltration to neighboring organs or extended to the thorax, with the aim of identifying the degree of dissemination of the tumor, but they are not systematically indicated, due to its high cost and

because it does not provide elements superior to those normally used.

**PET Scans:** Positron Emission Tomography (PET) scans track the movement of chemicals, respectively labeled, in the body. PET images are not as detailed as computed tomography (CT) scans, and cannot provide accurate information about the shape, size, and position of the tumor. PET scans can be used to identify the general location of the tumor, and the location of the cancer if it has metastasized.

**131I whole body scintigraphy** is the method used to assess the presence of residual normal or malignant thyroid tissue in the neck and/or distant metastases, and is only performed when TSH is high enough to stimulate good uptake and achieve a good image.

One cause for concern is that the high doses of 131I (a  $\beta$ -particle emitter) used in diagnostic screening may have an adverse effect on the uptake of the subsequent therapeutic dose, a phenomenon called "stunning" (reduced iodine uptake from previous exposure to low doses) [31-33].

In a study carried out in the General Surgery Service of the General Teaching Hospital "Dr. Juan Bruno Zayas Alfonso" of Santiago de Cuba. The means of diagnosis were analyzed, confirming that ultrasound is very useful for detecting these nodular thyroid lesions; Likewise, there was a high correspondence between the results of the CAAF and the histological diagnosis. On the other hand, frozen biopsy was a useful procedure in cases of negative or doubtful cytology, and the more radical the procedure, the greater the complications. 1, 2, 3 To diagnose thyroid cancer, it is essential to resort to complementary tests that confirm and typify the etiology together with the histology of the tumor.

## Conclusion

The neck nodule is considered the most frequent and most serious clinical finding of Thyroid cancer; Health professionals must appropriate the clinical and epidemiological method to know the classification of this disease, the type of cancer, the anatomopathological variety, the presence or absence of metastases, which reveals the need to indicate, perform and interpret complementary tests, depending on the scientific and technical availability of each laboratory. Therefore, CAAF, the determination of TSH in blood and high-resolution thyroid ultrasound are the most effective diagnostic means for the early detection of this neoplasm. This aspect is widely debated by multidisciplinary groups that deal with thyroid cancer, an alert is being carried out worldwide to work on the risk factors of this neoplasm to reduce incidence, prevalence and mortality.

## Conflicts of interest

The authors declare no conflicts of interest.

## Author's contribution:

Mary of Jesus George Bell. Idea of scientific work, model design, theoretical systematization. Review of the primary data and the bibliography, statistical report presentation of information and preparation of the final report.

Dr. Josefa Bell Castillo. Review of the primary data and the bibliography, statistical report and final review of the report. Collection and systematization

Dr. Wilberto George Carrión. Review of the primary data and the bibliography, statistical report and final review of the report. Collection and systematization.

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