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Benign Versus Malignant THYROID NODULES: US differentiation, with Tissue Diagnosis as standard reference

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In partial fulfillment of the requirements

For the award of the degree of

CLINICAL MD IN DIAGNOSTIC RADIOLOGY

BY

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وقل رب زدني

Dedication

To………

My father's soul may (Allah) blesses him.

My mother the greatest woman, may (Allah) blesses her.

Mywifeand son.

All my teachers & colleagues in radiology.

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I would like to gratefully thank my Teachers in Radiology board to their knowledge that they gave throughout my career. God keeps all of them

Abstract

Aim: This study aimed to evaluate the diagnostic accuracy of ultrasonographic (U/S) criteria for the depiction of benign and malignant thyroid nodules by using tissue diagnosis as the reference standard.

Materials & methods: U/S scans of patients with thyroid nodules having histopathology diagnosis in some of Khartoum state hospitals from December 2010 to July 2012.

Results: The study included 92 patients presented with thyroid nodules that had have U/S examination and underwent surgery with biopsy or FNAC. 74 patients (80.4%) were females, and 18 patients (19.6%) were males. The age of the patients was ranging from 17 to 85 years. 50 of the patients (54.3%) were having benign thyroid nodules and 42 (45.7%) were having malignant nodules. The study found that U/S features of benign thyroid nodules are: predominantly cystic component (sensitivity ***24.0%***, specificity ***95.2%***, positive predictive value ***85.7%***, and negative predictive value ***51.3%***), round to ovoid shape (sensitivity ***90.0%***, specificity ***54.8%***, positive predictive value ***70.3%***, and negative predictive value ***82.1%***), well- defined smooth margin (sensitivity ***84.0%***, specificity ***69.0%***, positive predictive value ***76.4%***, and negative predictive value ***78.4%***), isoechogenicity (sensitivity ***56.0%***, specificity ***90.5%***, positive predictive value ***87.5%***, and negative predictive value ***63.3%***), multinodularity (sensitivity ***76.0%***, specificity ***57.1%***, positive predictive value ***67.9%***, and negative predictive value***66.7%***), Absence of calcification (sensitivity***78.0%***, specificity ***57.1%***, positive predictive value ***68.4%***, and negative predictive value ***68.6%***) and perinodular vascularization (sensitivity ***38.0%***, specificity ***90.5%***, positive predictive value ***82.6%***, and negative predictive value ***55.1%***), while U/S features of malignant nodules are:taller thanwide shape (sensitivity ***33.3%***, specificity ***94.0%***, positive predictive value ***82.4%***, and negative predictive value ***62.7%***), irregular shape (sensitivity ***21.4%***, specificity ***96.0%***, positive predictive value ***81.8%***, and negative predictive value ***59.3%***), speculated margin (sensitivity ***52.4%***, specificity ***94.0%***, positive predictive value ***88.0%***, and negative predictive value ***70.1%***), Hypoechogenicity (sensitivity ***85.7%***, specificity ***64.0%***, positive predictive value***66.7%***, and negative predictive value***84.2%***), solitary nodule

(sensitivity ***57.1%***, specificity ***76.0%***, positive predictive value ***66.7%***, and negative predictive value ***67.9%***), Presence of microcalcification (sensitivity ***42.9%***, specificity ***96.0%***, positive predictive value ***90.0%***, and negative predictive value ***66.7%***), intranodular vascularization (sensitivity ***66.7%***, specificity ***78.0%***, positive predictive value ***71.8%***, and negative predictive value ***73.6%***) and Presence of regional enlarged lymph nodes (sensitivity ***33.3%***, specificity ***96.0%***, positive predictive value ***87.5%***, and negative predictive value ***63.2%***).

Conclusion: U/S features (shape, margins, echogenicity, presence of calcification, type of vascularization, multinodularity & presence of regional lymphadenopathy) were found to be helpful in discrimination of malignant from benign nodules specially when more than one feature are present.

ملخص الأطروحة

الهدف: تهدف الأطروحة إلى تقييم أهمية محددة لمميزات الموجات فوق الصوتية للتمييز بين عقيدات الغدة الدرقية الحميدة والخبيثة، باستخدام تشخيص الأنسجة كمعيار مرجعي.

المرضى وطريقة البحث: تم دراسة تقارير الموجات فوق الصوتية لمرضى يعانون من العقيدات الدرقية في بعض مستشفيات ولاية الخرطوم في الفترة من ديسمبر 2010 إلى يوليو 2012. ثم مقارنة صفات الموجات فوق الصوتية المحددة للعقيدات مع النتائج المعملية للأنسجة. ثم حساب القيم ذات الدلالة الاحصائية لصفات الموجات فوق الصوتية للعقيدات.

النتائج: شملت الدراسة 92 مريضا بعقيدات الغدة الدرقية 74 منهم كانوا نساءً و18 منهم رجال وكانت اعمار المرضى تتراوح بين 17-85 عاما. تم العثور على ملامح نسيجية حميدة للأورام في 50 حالة (54,3٪) وملامح نسيجية خبيث في 42 حالة (45,7٪). ووجد ان معظم مميزات الموجات فوق الصوتية للتنبؤ بتشخيص عقيدات الغدة الدرقية الحميدة كالتالي: التكوين الكيسي (حساسية 24%, خصوصية 95,2%, قيمة تنبؤية ايجابية 85,7% و قيمة تنبؤية سلبية 51,3%), بيضاوية ومستديرة الشكل (حساسية 90%, خصوصية 54,8%, قيمة تنبؤية ايجابية 70,3% و قيمة تنبؤية سلبية 82,1%), ذات هامش خارجي محدد بشكل جيد (حساسية 84%, خصوصية 69%, قيمة تنبؤية ايجابية 76,4% و قيمة تنبؤية سلبية 78,4%), صدوية متجانسة (حساسية 56%, خصوصية 90,5%, قيمة تنبؤية ايجابية 87,5% و قيمة تنبؤية سلبية 63,3%), العقيدات المتعددة (حساسية 76%, خصوصية 57,1%, قيمة تنبؤية ايجابية 67,9% و قيمة تنبؤية سلبية 66,7%), عدم وجود تكلس (حساسية 78%, خصوصية 57,1%, قيمة تنبؤية ايجابية 68,4% و قيمة تنبؤية سلبية 68,6%), وجود اوعية دموية حول العقيدات (حساسية 38%, خصوصية 90,5%, قيمة تنبؤية ايجابية 82,6% و قيمة تنبؤية سلبية 55,1%), ووجد ان معظم مميزات الموجات فوق الصوتية للتنبؤ بتشخيص عقيدات الغدة الدرقية الخبيثة كالتالي: أبعاد أعمق من أعرض (حساسية 33,3%, خصوصية 94%, قيمة تنبؤية ايجابية 82,4% و قيمة تنبؤية سلبية 62,7%), غير منتظم الشكل (حساسية 21,4%, خصوصية 96%, قيمة تنبؤية ايجابية 81,8% و قيمة تنبؤية سلبية 59,3%), ذات حواف مسننة و نتوءات خارجية (حساسية 52,4%, خصوصية 94%, قيمة تنبؤية ايجابية 88% و قيمة تنبؤية سلبية 70,1%), نقصان الصدوية (حساسية 85,7%, خصوصية 64%, قيمة تنبؤية ايجابية 66,7% و قيمة تنبؤية سلبية 84,2%), وجود عقيدة واحدة (حساسية 57,1%, خصوصية 76%, قيمة تنبؤية ايجابية 66,7% و قيمة تنبؤية سلبية 67,9%), وجود حبيبات تكلس صغيرة (حساسية 42,9%, خصوصية 96%, قيمة تنبؤية ايجابية 90% و قيمة تنبؤية سلبية 66,7%), وجود أوعية دموية داخل العقيدة (حساسية 66,7%, خصوصية 78%, قيمة تنبؤية ايجابية 71,8% و قيمة تنبؤية سلبية 73,6%) و وجود عقد لمفاوية عنقية متضخمة (حساسية 33,3%, خصوصية 96%, قيمة تنبؤية ايجابية 87,5% و قيمة تنبؤية سلبية 63,2%).

الخاتمة: وجد أن بعض صفات الموجات فوق الصوتية لعقيدات الغدة الدرقية مفيدة في تمييز العقيدات الخبيثة من العقيدات الحميدة خاصة عند وجود أكثر من صفة واحدة.

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List of ABBREVIATIONS

CT: computed tomography

FNAC: fine needle aspiration cytology

MEN: multiple endocrine neoplasia

MHz: mega Hertz

MRI: magnetic resonance imaging

QJM: An International Journal of Medicine: OxfordJournals

RSNA: Radiological Society of North America

SPSS: statistical package for social sciences

US: ultrasound\ultrasonography

Chapter one

Introduction

Objectives & Justifications

Literatur ereview

Introduction

Thyroid nodules are common, perhaps existing in almost half the population, as determined using ultrasonography (US). Only 4-7% of thyroid nodules detected with (US) are palpable in the adult population, with women affected more frequently than men.

Although the thyroid is the most common endocrine organ to undergo malignant degeneration, thyroid carcinoma accounts for only 1% of diagnosed neoplasms each year. [1,2] Thyroid cancer is rare; the annual detection rate of clinically significant thyroid cancer in the general population is only 0.004%. Only 5-10% of thyroid cancers are clinically palpable. [3,4]

Among asymptomatic patients, 7-21% have palpable nodules found on routine clinical examination. (US) can be used to identify many more nonpalpable nodules, and it can depict thyroid cysts as small as 2 mm and solid nodules as small as 3 mm. [5,6]

Sonograms in 40% of the general adult population demonstrate single or multiple nodules. In an autopsy series, 49% of patients who had had clinically normal thyroid glands were found to have one or more grossly visible nodules, where as the incidence of malignancy in the same autopsy series was 2-4%. [7,8]

At examination, the challenge is to differentiate the few clinically significant nodules from the many benign ones. Thyroid nodules are usually clearly identified by using US. No single US criterion is reliable for differentiating all benign thyroid nodules from malignant ones, but many US features may aid in predicting the benign or malignant nature of a given nodule. [9,10,11,12,13]

Usually, US is the first modality used to investigate a palpable thyroid nodule and in searching for a primary lesion in a patient with systemic metastases. US may be the only examination required in cases of hemorrhagic cyst and multinodular goiter. Doppler US is an extension of US and provides valuable information regarding the vascularity of nodules. Most intervention in the thyroid, such as fine-needle aspiration (FNA) and guided thyroid ablation, are performed under US guidance.

Currently, scintigraphy is reserved for characterizing functioning nodules and for staging follicular and papillary carcinomas. Lymphoma of the thyroid is the only gallium-67–avid thyroid nodule.

Plain radiographs are used to detect retrosternal thyroid extension, thyroid calcification, bony or mediastinal lymph nodes, and lung metastases.

Computed tomography (CT) scanning is an effective method for detecting regional and distant metastasis from thyroid cancer.

At the present time, magnetic resonance imaging (MRI) has a limited role in characterizing thyroid nodules, although it appears to be effective in the diagnosis of cervical lymph node metastasis.

Percutaneous needle aspiration remains the key procedure in the diagnosis of thyroid lymphoma; however, thyroid lymphoma's differentiation from thyroiditis occasionally can be difficult. US helps in diagnosing thyroid lymphoma most accurately, and CT helps in staging the disease most accurately. However, MRI also can be useful in staging the lymphoma. A tissue-specific diagnosis of a lymphoma can be achieved by using US-guided FNA. [14, 15]

Objectives

1- To evaluate (prospectively & retrospectively) the diagnostic accuracy of ultrasonographic (U/S) criteria for the depiction of benign and malignant thyroid nodules by using tissue diagnosis as the reference standard.

2- To determine whether thyroid nodules that diagnosed as probably benign at U/S can be used in clinical decision-making.

Literature review

Embryological consideration:

The thyroid gland is the first of the body's endocrine glands to develop, approximately at the 3–4 weeks of gestation**.** The gland originates as a proliferation of endodermal epithelial cells on the median surface of the developing pharyngeal floor. The site of this initial development lies between two key structures, the *tuberculum impar* and the *copula*, and is known as the *foramen cecum*. The thyroid initially develops caudal to the *tuberculumimpar*, which is also known as the median tongue bud. This embryonic swelling arises from the first pharyngeal arch and occurs midline on the floor of the developing pharynx, eventually helping form the tongue as the 2 lateral lingual swellings overgrow it.

The *foramen cecum* begins rostral to the *copula*, also known as the *hypobranchial eminence*. This median embryologic swelling consists of mesoderm that arises from the second pharyngeal pouch (although the third and fourth pouches are also involved). The thyroid gland, therefore, originates from between the first and second pouches.

The initial thyroid precursor, the *thyroid primordium*, starts as a simple midline thickening and develops to form the thyroid diverticulum. This structure is initially hollow, although it later solidifies and becomes bilobed. The 2 lobes are located on either side of the midline and are connected via an isthmus.

The initial descent of the thyroid gland occurs anterior to the pharyngeal gut. At this point, the thyroid is still connected to the tongue via the *thyroglossal duct*. The tubular duct later solidifies and subsequently obliterates entirely (during gestational weeks 7-10). Nonetheless, in some individuals, remnantsof this duct may persist.

The *foramen cecum* represents the opening of the thyroglossal duct into the tongue; its remains may be observed as a small blind pit in the midline between the anterior two thirds and the posterior third of the tongue.

A pyramidal lobe of the thyroid may be observed in as many as 50% of patients. This lobe represents a persistence of the inferior end of the *thyroglossal duct* that has failed to obliterate. As such, the pyramidal lobe itself may be attached to the hyoid bone, similar to a thyroglossal duct cyst, or may be incorporated into a thyroglossal duct cyst.

Further descent of the thyroid gland carries it anteriorto the hyoid bone and, subsequently, anterior to the laryngeal cartilages. As the thyroid gland descends, it forms its mature shape, with a median isthmus connecting two lateral lobes. The thyroid completes its descent in the seventh gestational week, coming to rest in its final location immediately anterior to the trachea.

Parafollicular cells are also known as C cells. These cells are a special subset of cells within the thyroid gland that secrete calcitonin, a hormone necessary for the regulation of calcium.

The *parafollicular cells* arise from the *ultimobranchial body*. This body represents the last structure derived from the *branchial pouches*, hence its name. The ultimobranchial body arises from the fifth pharyngeal pouch, which is alternately described as the ventral portion of the fourth pharyngeal pouch. (Whether fifth pharyngeal pouches actually exist is debatable.)

Migrating cells from the neural crest region infiltrate the ultimobranchial body. This structure is then incorporated into the thyroid gland, as the ultimobranchial body fuses with the thyroid gland and disseminates its cells into it. The C cells of the thyroid, therefore, are of neural crest origin.

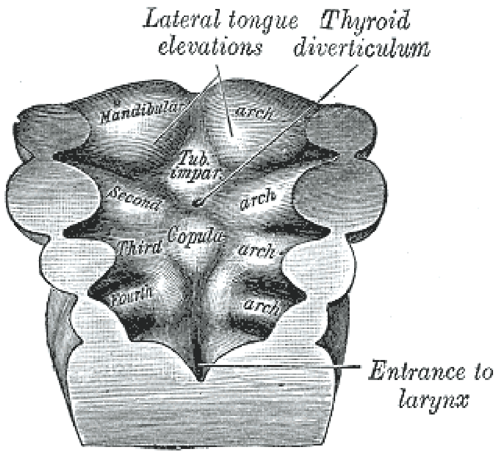


Fig1: Development of the thyroid gland

Thyroid Embryology Clinical Correlations:

If the thyroglossal duct does not atrophy, then the remnant can manifest clinically as a thyroglossal duct cyst. While half of these generally midlinecystic masses are located at or just below the level of the hyoid bone, they may be located and can track anywhere from the thyroid cartilage up the base of the tongue. If the cyst ruptures, it may go on to form a thyroglossal duct sinus or a thyroglossal duct fistula that exits through the overlying skin. Because the hyoid bone develops in an anterior direction and may surround the thyroglossal duct, the surgeon should resect the central portion on the hyoid bone along with the cyst (the Sistrunk procedure), unless the thyroglossal duct tract can clearly be observed coursing away from the bone [16].

An aberrant or ectopic thyroid gland may occur anywhere along the path of initial descent of the thyroid, although it is most common at the base of the tongue, just posterior to the foramen cecum. In this location, an aberrant or ectopic thyroid gland is known as a lingual thyroid and represents a failure of the thyroid to descend. This failure to descend contrasts with the incomplete descent of the thyroid, in which case the resulting final resting point of the gland may be high in the neck or just below the hyoid bone [17].

Accessory thyroid tissue can also occur, arising from remnants of the thyroglossal duct. While the accessory thyroid tissue may be functional, it is generally insufficient for normal function if the main thyroid gland is entirely removed. This accessory tissue may appear anywhere along the path of the thyroglossal duct tract.

Anatomy of the thyroid gland:

Overview

The thyroid is a highly vascular, brownish-red gland located anteriorly in the lower neck, extending from the level of the fifth cervical vertebra down to the first thoracic. The gland varies from an H to a U shape and is formed by two elongated lateral lobes with superior and inferior poles connected by a median isthmus, with an average height of *12-15 mm*, overlying the second to fourth tracheal rings. The isthmus is encountered during routine tracheotomy and must be retracted (superiorly or inferiorly) or divided. Occasionally, the isthmus is absent, and the gland exists as two distinct lobes. [18,19]

Each lobe is *50-60 mm* long, with the superior poles diverging laterally at the level of the oblique lines on the laminae of the thyroid cartilage. The lower poles diverge laterally at the level of the fifth tracheal cartilage. Although thyroid weight varies, it averages *25-30 g* in adults (it is slightly heavier in women). The gland enlarges during menstruation and pregnancy.

A conical pyramidal lobe often ascends from the isthmus or the adjacent part of either lobe (more often the left) toward the hyoid bone, to which it may be attached by a fibrous or fibromuscular band, the levator of the thyroid gland. Remnants of the thyroglossal duct may persist as accessory nodules or cysts of thyroid tissue between the isthmus and the *foramen caecum* of the tongue base. Usually, two pairs of parathyroid glands lie in proximity to the thyroid gland.

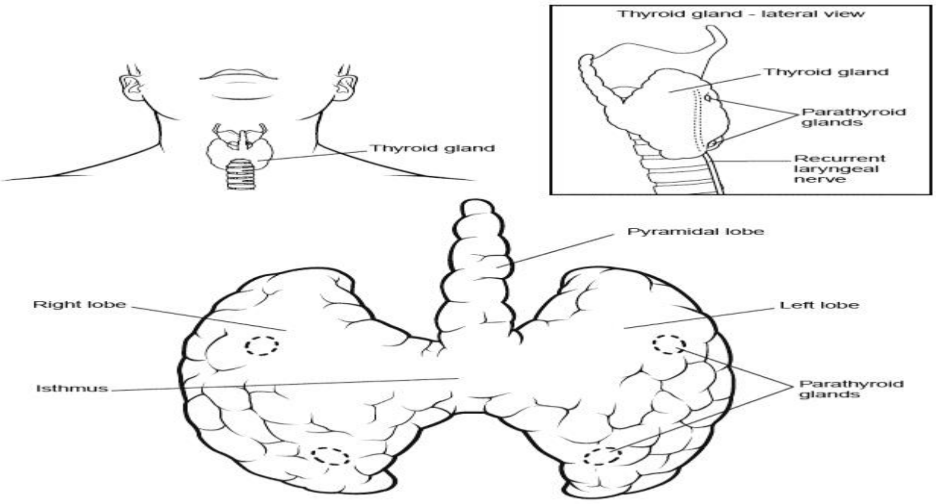


Fig2: Thyroid gland anterior and lateral views

Innervation of the thyroid

Principal innervation of the thyroid gland derives from the autonomic nervous system. Parasympathetic fibers come from the *vagus nerves*, and sympathetic fibers are distributed from the superior, middle, and inferior ganglia of the sympathetic trunk. These small nerves enter the gland along with the blood vessels. Autonomic nervous regulation of the glandular secretion is not clearly understood, but most of the effect is postulated to be on blood vessels, hence the perfusion rates of the glands.

Structure

Under the middle layer of deep cervical fascia, the thyroid has an inner true capsule, which is thin and adheres closely to the gland. Extensions of this capsule within the substance of the gland form numerous septae, which divide it into lobes and lobules. The lobules are composed of follicles, the structural units of the gland, which consist of a layer of simple epithelium enclosing a colloid-filled cavity.

This colloid contains an iodinated glycoprotein, *iodothyroglobulin*, aprecursor of thyroid hormones. Follicles vary in size, depending upon the degree of distention, and they are surrounded by dense plexuses of fenestrated capillaries, lymphatic vessels, and sympathetic nerves.

Epithelial cells are of two types: principal cells (ie, *follicular*) and parafollicular cells (ie, *C, clear, light cells*). Principal cells are responsible for formation of the colloid (iodothyroglobulin), whereas parafollicular cells produce the hormone calcitonin, a protein central to calcium homeostasis. Parafollicular cells lie adjacent to the follicles within the basal lamina.

Fascia and Ligament

The thyroid gland is ensheathed bythevisceral fascia, adivision ofthe middle layer of deep cervical fascia, which attaches it firmly to the laryngoskeleton. The anterior suspensory ligament extends from the superior-medial aspect of each thyroid lobe to the cricoid and thyroid cartilage. The posteromedialaspect of the gland is attached to the side of the cricoid cartilage, first and second tracheal ring, by the posterior suspensory ligament (ie, *Berryligament*). This firm attachment of the gland to the laryngoskeleton is responsible for movement of the thyroid gland and related structures during swallowing.

On its way to the larynx, the recurrent laryngeal nerve usually passes deep to the Berry ligament or between the main ligament and its lateral leaf. Deep to the ligament, but lateral to the nerve, is a posteromedial portion of the thyroid lobe, which may be overlooked during thyroidectomy.

StrapMuscles

The lateral surface of the thyroid is covered by the *sternothyroid* muscle, and its attachment to the oblique line of the thyroid cartilage prevents the superior pole from extending superiorly under the *thyrohyoid* muscle. More anteriorly are the *sternohyoid* and superior belly of the *omohyoid* muscle, overlapped inferiorly by the anterior border of the *sternocleidomastoid* muscle. The *sternohyoid* and *sternothyroid* muscles are joined in the midline by an avascular fascia that must be incised to retract the strap muscle laterally in order to access the thyroid gland during thyroidectomy. If strap muscles are to be transected for better exposure, do so high in the neck, because the motor nerve supply from the *ansa cervicalis* enters these muscles inferiorly.

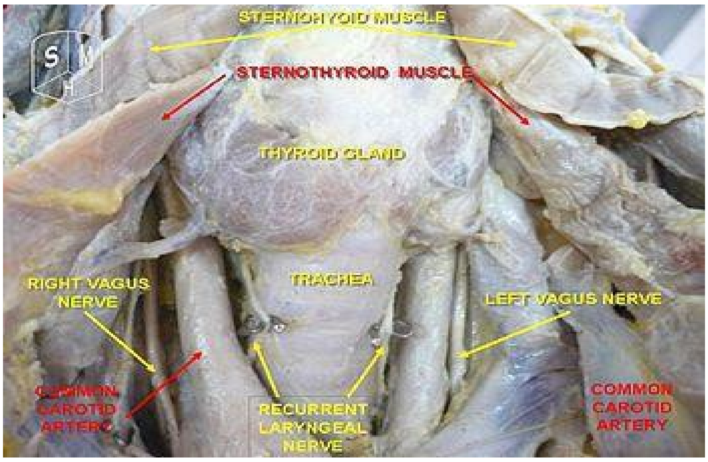


Fig3: Thyroid gland

Vascular Anatomy and Laryngeal Innervation

The arterial supply to the thyroid gland comes from the superior and inferior thyroid arteries and, occasionally, from the *thyroideaima*. These arteries have abundant collateral anastomoses with each other, ipsilaterally and contralaterally. The *thyroid ima*is a single vessel that, when present, originates from the aortic arch or the *innominate artery* and enters the thyroid gland at the inferior border of the isthmus.

Superior thyroid artery and superior laryngeal nerve

The superior thyroid artery is the first anterior branch of the external carotid artery. In rare cases, it may arise from the common carotid artery just before its bifurcation. The superior thyroid artery descends laterally to the larynx under the cover of the omohyoid and sternohyoid muscles. The artery runs superficially on the anterior border of the lateral lobe, sending a branch deep into the gland before curving toward the isthmus, where it anastomoses with the contralateral artery.

Cephalad to the superior pole, the external branch of the superior laryngeal nerve runs with the superior thyroid artery before turning medially to supply the cricothyroid muscle. High ligation of the superior thyroid artery during thyroidectomy places this nerve at risk of inadvertent injury, which would produce *dysphonia* by altering pitch regulation. The cricothyroid artery, a potentially bothersome branch of the superior thyroid artery, runs cephalad to the upper pole and runs toward the midline on the cricothyroid ligament. This vessel can be lacerated during emergent cricothyroidotomy [20].

Inferior thyroid artery and recurrent laryngeal nerve

The inferior thyroid artery arises from the *thyrocervical trunk*, a branch of the *subclavian artery*. It ascends vertically and then curves medially to enter the tracheoesophageal groove in a plane posterior to the carotid sheath. Most of its branches penetrate the posterior aspect of the lateral lobe.

The inferior thyroid artery has a variable branching pattern and is closely associated with the recurrent laryngeal nerve. The latter also ascends in the tracheoesophageal groove and enters the larynx between the inferior cornu of the thyroid cartilage and the arch of the cricoid. The recurrent laryngeal nerve can be found after it emerges from the superior thoracic outlet, in a triangle bounded laterally by the common carotid artery, medially by the trachea, and superiorly by the thyroid lobe.

The relationship between the nerve and the inferior thyroid artery is highly variable, as demonstrated by the classic work of Reed, who in 1943 described 28 variations in this relationship. The nerve can be found deep to the inferior thyroid artery (40%), superficially (20%), or between branches of the artery (35%) [21]. Significantly, the relationship between nerve and artery on one side of the neck is similar to that found on the other side in only 17% of the population. Furthermore, at the level of the inferior thyroid artery, branches of the recurrent laryngeal nerve that are extralaryngeal may be present (5%). Preservation of all of those branches is important during thyroidectomy.

Another hint to the location of the recurrent laryngeal nerve is the *Zuckerkandl tubercle*, an extension of the thyroid, which is close to the Berry ligament [22]. On rare occasions, the recurrent laryngeal nerve may pass directly from the vagus to the larynx, close to the superior thyroid vessels.This formation is nearly always observed on the right side and is associated with a retroesophageal subclavian artery. However, the formation can occuron the left side in cases of transposition of the great vessels.

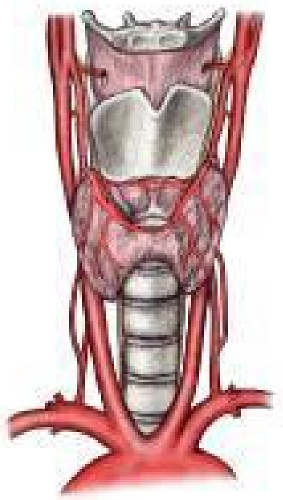


Fig4: Distribution of thyroid arteries with associated laryngeal nerve, anterior view.

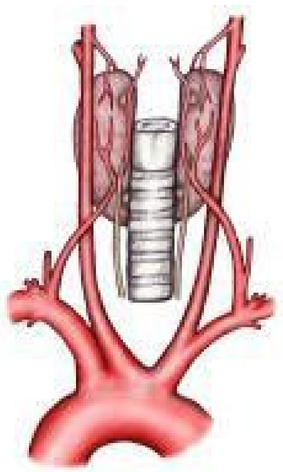


Fig5: Distribution of thyroid arteries with associated laryngeal nerve, posterior view.

Venous Drainage and Lymphatics

Three pairs of veins provide venous drainage for the thyroid gland. The superior thyroid vein ascends along the superior thyroid artery and becomes a tributary of the internal jugular vein. The middle thyroid vein follows a direct course laterally to the internal jugular vein. The inferior thyroid veins follow different paths on each side. The right passes anterior to the innominate artery to the right brachiocephalic vein or anterior to the trachea to the left brachiocephalic vein. On the left side, drainage is to the left brachiocephalic vein. Occasionally, both inferior veins form a common trunk called thethyroid ima vein, which empties into the left brachiocephalic vein.

Fig6: Distribution of thyroid veins.

Lymphatic drainage of the thyroid gland is extensive and flows multidirectionally. Immediate lymphatic drainage courses to the periglandular nodes; to the prelaryngeal *(Delphian)*, pretracheal, and paratracheal nodes along the recurrent laryngeal nerve; and then to mediastinal lymph nodes. Regional metastases of thyroid carcinoma can also be found laterally, higherin the neck along the internal jugular vein. This can be explained by tumor invasion of the pretracheal and paratracheal nodes causing an obstruction of normal lymph flow.

Evaluation of Thyroid Nodules:

Overview

Nodular disorders of the thyroid gland are relatively common among adults. Most thyroid nodules are benign hyperplastic lesions, but ***5-20%*** of thyroid nodules are true neoplasms. One of the major goals in the evaluation of the solitary thyroid nodule is the differentiation of hyperplasia from true neoplasms. Furthermore, the histological criteria used to distinguish benign from malignant neoplasms can be subtle. Evaluation of thyroid nodules requires the collaboration of the primary care physician, endocrinologist, pathologist, radiologist, and head and neck surgeon to provide comprehensive and appropriate management of this clinical entity.

The prevalence of thyroid nodules within a given population depends on a variety of factors that include age, sex, diet, iodine deficiency, and therapeutic and environmental radiation exposure. Thyroid nodules are found in approximately 1.5% of children and adolescents. They are more common in females, and this predisposition exists throughout all age groups. In fact, palpable nodular disease is 6 times more common in adolescent females compared to males of the same age.

Thyroid nodules are more common in women than in men. Prevalence increases with age, with spontaneous nodules occurring at a rate of 0.08% per year beginning early in life and extending into the eighth decade. Thyroid nodules are found in 5% of persons aged an average of 60 years.

Ultrasound features of thyroid nodules

The vast majority of thyroid nodules are benign, and the role of a radiologistin assessment of the thyroid gland is to differentiate a malignant thyroid nodulefromthe more commonlyseen benign ones. It is therefore important to evaluate the sonographic features of thyroid nodules as these aid in their characterization.

1- *Echogenicity:*
The incidence of malignancy is 4% when a solid thyroid nodule is hyperechoic. If the lesion is hypoechoic the incidence of malignancy rises to 26% [23]. However, hypoechogenicity alone is inaccurate in predicting malignancy, and if used as a sole predictive sign, it has a relatively poor specificity (49%) and positive predictive value (40%) [24].

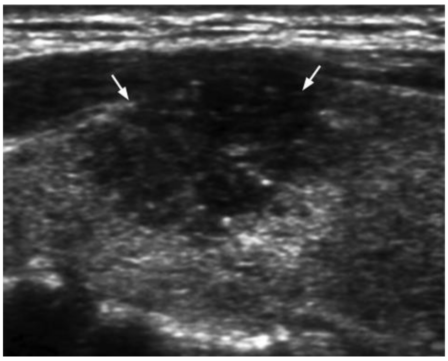


Fig7: Longitudinal grey scale sonogram shows a solid, hypoechoic thyroidnodule (arrows) with ill-defined margins anteriorly. Histology: papillary carcinoma.

2- *Shape:*
Malignant nodules tend take the shape of taller than wide or irregular shape while benign nodules tend to be ovoid or round.

3- *Margins:*

A malignant thyroid nodule tends to have ill-defined margins or speculated margins on ultrasound (*Fig 7*). A peripheral halo of decreased echogenicity is seen around hypoechoic and isoechoic nodules and is caused byeither the capsule of the nodule or compressed thyroid tissue and vessels [25].

4- *Calcification*:
Fine punctate calcification due to calcified psammoma bodies withinthe nodule is seen in papillary carcinoma in 25%–40% of cases [26]. If used as the sole predictive sign of malignancy, microcalcification is the most reliable one [24]. Coarse, dysmorphic or curvilinear calcifications commonly indicate benignity.

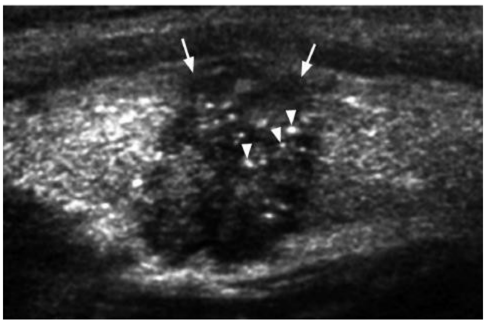


Fig8: Longitudinal grey scale sonogram shows characteristic punctate calcification (arrowheads) within an ill-defined solid hypoechoic thyroid nodule (arrows) which is highly suggestive of papillary carcinoma.

Fig9: Longitudinal grey scale sonogram shows coarse calcifications (arrows) with dense shadowing within a thyroid nodule suggestive of benign calcification.

5- *Comet-tail sign*:
The presence of a comet tail sign in a thyroid nodule indicates the presence of colloid within a benign colloid nodule [27] and is a strong predictor of benignity.

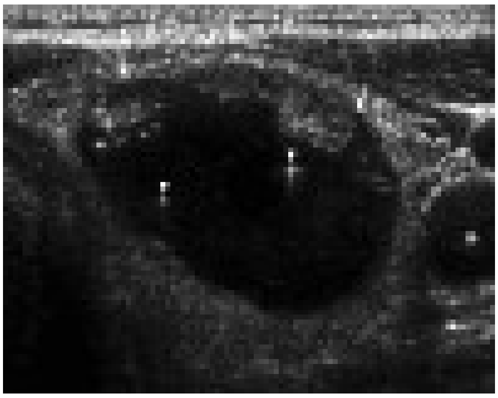


Fig 10: Transverse grey scale sonogram shows the presence of comet-tail artifacts (arrowheads) within a predominantly cystic thyroid nodule (arrows). Features are of a benign colloid nodule.

6- *Solid/cystic*:
It is generally believed that thyroid nodules with large cystic components are usually benign nodules that have undergone cystic degeneration or haemorrhage. However, papillary carcinoma occasionally demonstrates a cystic component and may mimic a benign nodule, though the presence of punctate calcification within the solid component helps in its identification.

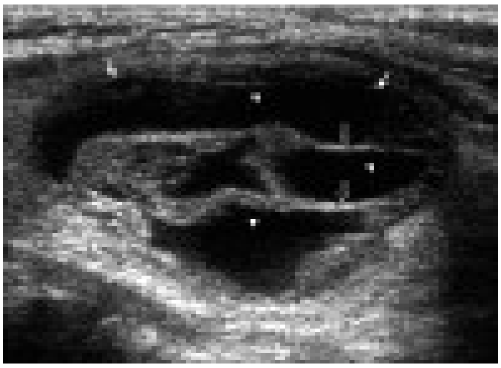


Fig 11: Longitudinal grey scale sonogram shows a well-defined heterogeneous thyroid nodule (arrows) with a large cystic component (arrowheads) and septation (openarrows). Features are compatible with a benign hyperplastic nodule.

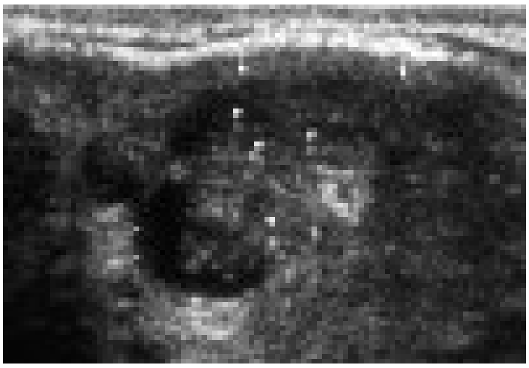


Fig12: Transverse grey scale sonogram shows a cystic component (openarrows) within a papillary carcinoma (arrows) of the thyroid. The presence of punctate calcification (arrowheads) identifiesits malignant nature.

7- *Multinodularity:*

It is a myth that multinodularity implies benignity, as approximately 10%–20% of papillary carcinomas may be multicentric [25,28]. In those with true solitary nodules confirmed at surgery the risk of cancer is the same as in those with multinodular goiters [29]. Therefore, against a background of multinodular changes, extra caution should be taken not to miss a suspicious nodule.

8- *Colour flow patterns*:

In general, there are three patterns of vascular distribution within a thyroid nodule [30]:

- TypeI: complete absence of flow signal within the nodule
- TypeII: exclusive perinodular flow signals
- TypeIII: intramodular flow with multiple vascular poles chaotically arranged, with or without significant perinodular vessels.

Type III pattern is generally associated with malignancy. Types I and II are more commonly seen in benign hyperplastic nodules [30,31]. Unfortunately, if used as the sole predictor of malignancy [32], colour flow characteristics are not accurate, and have to be used in combination with other features seen on grey scale ultrasound.

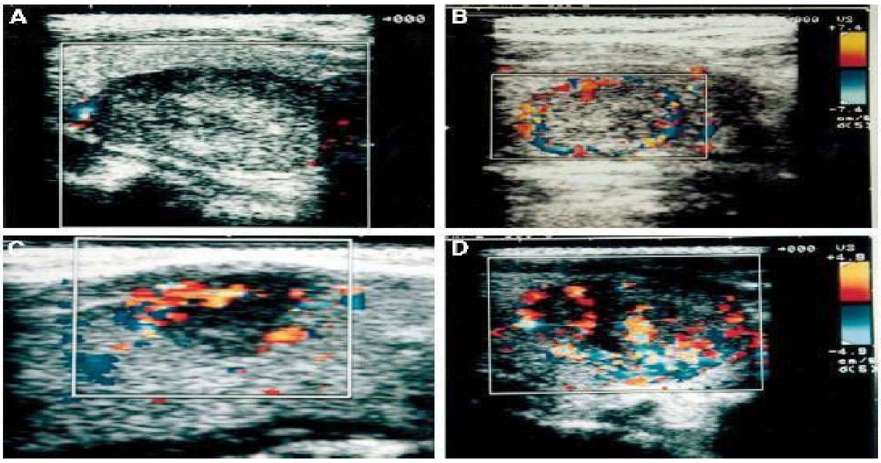


Fig13: Color flow-Doppler sonographic patterns. A: absence of blood flow (TypeI). B: perinodular blood flow (TypeII). C: slight intramodular blood flow (TypeIII). D: marked intranodular blood flow (Type III).

It is well recognized that the predictive ability of ultrasound for malignancy is effective only when multiple signs are present in the same nodule. Although their predictive value increases in summation, it is at the cost of sensitivity.

Benign Thyroid Nodules

Thyroid adenomas

Thyroid adenomas are benign neoplasms, which are usually classified as follicular or papillary. Follicular adenomas are the most common type of adenomas and arise from the follicular epithelium within the thyroid gland. They are typically homogeneous, solitary, and encapsulated tumors that are histologically distinct from adjacent thyroid tissue. Follicular adenomas are further classified according to their cellular architecture and relative amounts of cellularityand colloid into *fetal* (*microfollicular*), *colloid* (*macrofollicular*), *embryonal* (*atypical*), and *Hürthle*(*oxyphil*) cell types. Colloid adenomas do not have any potential for microinvasion, while the fetal, embryonal, and Hürthle cell adenomas all have the potential for microinvasion. Papillary adenomas are the least common type of thyroid adenoma.

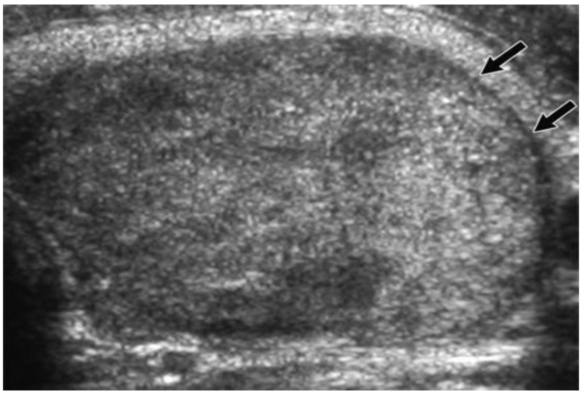


Fig14: Follicular adenoma in 30 yrs old woman

Hyper plastic nodules

Hyperplastic nodules can be differentiated from colloid goiters by the presence of excessive cellularity, acinar formation, marginal vacuoles, papillary formation, and the amount of colloid present in the specimen. Neoplasms have a higher degree of papillary formation, intranuclear inclusions and nuclear grooves, and fewer marginal vacuoles. Congenital thyroid nodules include congenital hemangioma, thyroglossal duct anomalies, and familial disorders, such as multiple endocrine neoplasia (MEN) syndromes and congenital goitrous hypothyroidism.

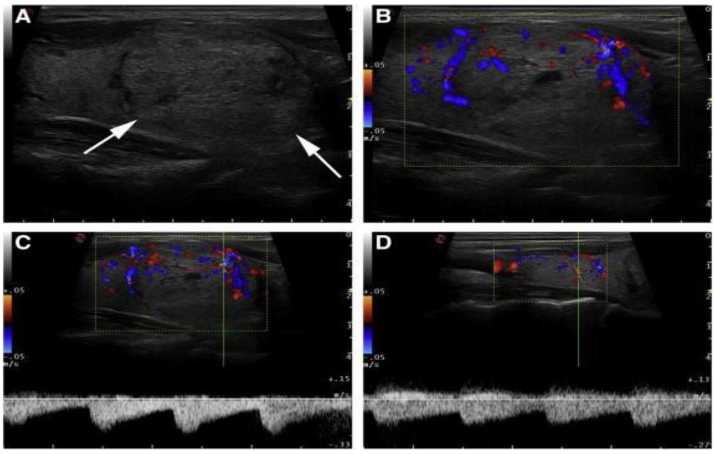


Fig15: hyperplastic nodule in 52 yrs old man

Thyroid cysts

Thyroid cysts represent 15-25% of all thyroid nodules and are usually diagnosed by the aspiration of fluid from a solitary thyroid nodule. These entities are often caused by cystic degeneration of normal thyroid tissue, hemorrhage or trauma, occult follicular adenoma or carcinoma, multinodular goiter, or branchial anomalies that involve the thyroid gland. Simple epithelium-lined cysts, hemorrhagic colloid nodules, or necrotic papillary thyroid cancers can be found in resection specimens. In one particular study, 68% of cystic thyroid lesions selected for surgical therapy were benign, while 32% were thyroid carcinomas. To improve the diagnostic accuracy of aspiration biopsy, some authors advocate biochemical analysis of cyst fluid.

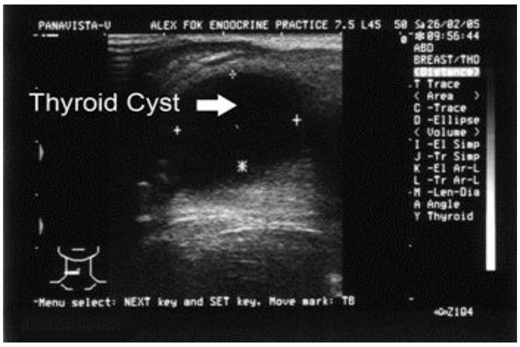


Fig16: thyroid cyst

Thyroiditis

Diagnosis of thyroiditis includes five disorders. *Hashimoto thyroiditis*is an autoimmune disease; principal manifestations are goiter and hypothyroidism. *Subacute granulomatous thyroiditis* is probably viral in origin, and patients usually present with a tender goiter. *Subacute lymphocytic thyroiditis* is of unknown pathogenesis, but the postpartum form may be autoimmune. Its principal manifestations are goiter and spontaneously reversible hyperthyroidism.

Acute suppurative thyroiditis results frombacterial or fungal infection causing abscess. *Riedel struma*, a disease of unknown cause, manifests with a goiter and thoracic inlet obstruction. The presence of clinical or metabolic hyperthyroidism in combination with painful nodular thyroid disease strongly suggests thyroiditis as a potential diagnosis. Local abscess is usually infectious, but it may develop from necrotic undifferentiated thyroid carcinoma. Infectious etiologies include bacterial, viral, fungal, and parasitic sources, or it could be the result of piriform sinus fistula [33,34].

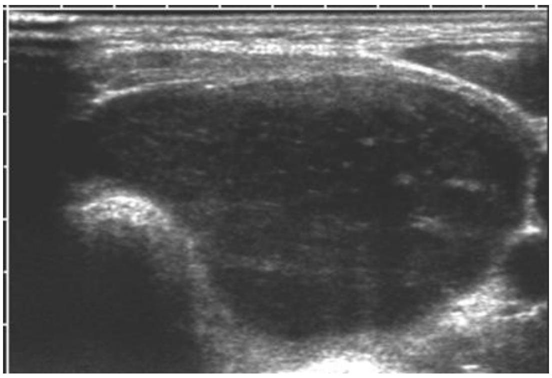


Fig17: Diffusely enlarged heterogeneous hypoechoic thyroid in Pt with Hashimoto's thyroiditis.

Malignant Thyroid Nodules

Papillary carcinoma

Papillary carcinoma accounts for 60%–70% of all thyroid malignancies [35], with a peak incidence in the third and fourth decades. Females are more commonly affected than males. The tumour commonly spreads along the rich lymphatic system within and adjacent to the thyroid gland accounting for the multifocal nature of the tumour within the thyroid gland and its spread to regional lymph nodes. Venous invasion occurs in 7% of papillary carcinomas and distant metastases to bone and lung are seen in 5%–7% [36].

Ultrasound features of papillary carcinoma include:

- Predominantly solid (70%) and hypoechoic (77%–90%) [26,31].
- Presence of punctate microcalcification (25%–90%) [26,31], correspond to psammomas bodies on microscopy.
- Ill-defined margins [37,38].
- Chaotic intramodular vascularity on colour flow imaging [31].
- Adjacent characteristic lymph nodes [39]: cystic necrosis in 25%, microcalcification in 50%, located in the pre-/paratracheal regions and along the cervical chains.

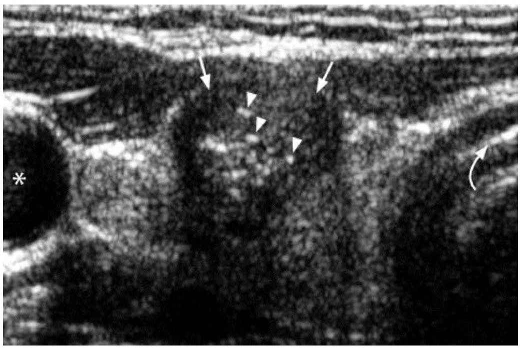


Fig18: Transverse grey scale sonogram shows a solid, ill-defined, hypoechoic nodule (arrows) containing punctate calcification (arrowheads) in the right lobe of thyroid gland. Features are typical of papillary carcinoma of thyroid.

Anaplastic carcinoma

Anaplastic carcinoma is one of the most aggressive head and neck cancers and has a grave prognosis. It accounts for 15%–20% of all thyroid cancers [35]. The diagnosis is suspected clinically with rapid growth in a long-standing thyroid nodule. Patients frequently present with signs and symptoms of airway compression.

Ultrasound features of anaplastic carcinoma include:

- Hypoechoic tumour diffusely involving the entire lobe or gland.
- Ill-defined margin.
- Areas of necrosis in78% [26].
- Nodal or distant metastases in 80% of patients [40,41]; the involved lymph nodes show evidence of necrosis in 50% [26].
- Multiple small intramodular vessels on colour flow imaging.
- Extracapsular spread and vascular invasion in a third of patients [40,41].

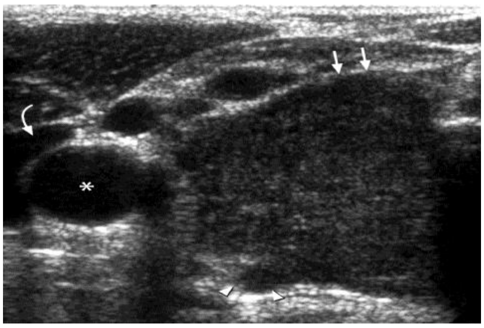


Fig19: Transverse grey scale sonogram shows a large, solid, hypoechoic mass (arrows) occupying the right lobe of thyroid gland. Note the presence of extra-thyroid spread posteriorly (arrowheads). Histology: anaplastic carcinoma.

Medullary carcinoma

Medullary carcinoma is believed to arise from parafollicular C-cells that secrete thyrocalcitonin. It represents 5% of all thyroid cancers [35]. In 10%– 20% of all cases there is a family history of pheochromocytoma or hypercalcaemia. At presentation, 50% of cases have nodal metastases and 15%–25% have distant metastases to liver, lungs and bone [36]. Medullary carcinoma may be associated with MEN syndrome, and these patients have a biologically more aggressive tumour and may develop metastases earlier with a 55% 5-year survival rate [42,43]. Recurrence in the neck and mediastinum is common in medullary carcinoma and is reflected biochemically withincreased serum calcitonin levels.

Ultrasound features of medullary carcinoma include:

- Solid hypoechoic nodule.
- Echogenic foci in 80–90% of tumours due to amyloid deposition and associated calcification [26,35]; similar deposits are also seen in 50–60% of associated nodal metastases.
- Chaotic intramodular vessels within the tumour on colour flow imaging.

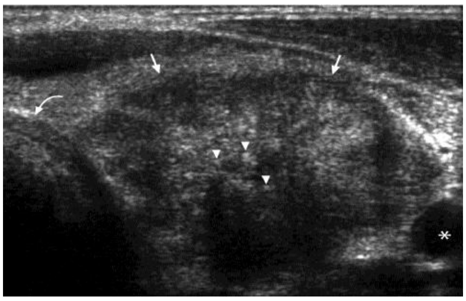


Fig 20: Transverse grey scale sonogram shows an ill-defined, solid, hypoechoic mass (arrows) occupying the left lobe of the thyroid gland. Multiple echogenic foci (arrowheads) casting dense posterior acoustic shadowing probably related to amyloid deposition and associated calcification. Appearance is that of a medullary carcinoma.

Follicular lesions

A follicular thyroid lesion comprises follicular adenoma and follicular carcinoma which can only be distinguished on histology of the surgical specimen by the presence/absence of vascular and capsular invasion. Therefore, it is often not possible to differentiate a benign from a malignant follicular lesion with FNAC or core biopsy. Some clinicians therefore preferto use the collective term ‘follicular lesion’ for both a benign follicular adenoma and a malignant follicular carcinoma.

Although it is not possible to differentiate benign from malignant follicular lesion on FNAC/core biopsy, some cytologists will try and classify these into microfollicular and macrofollicular types. The latter is associated with a low risk of carcinoma, whereas in 20%–25% a microfollicular lesion may be a follicular carcinoma [44].

A follicular carcinoma accounts for 2%–5% of all thyroid cancers [34] and is more prevalent (25%–30%) in iodine deficient areas [45]. In most cases it develops from a pre-existing adenoma and has propensity for haematogenous metastases to lungs, liver, bone and brain. Nodal metastases in the neck are less commonly encountered.

Ultrasound features of follicular lesions include:

- Hyperechoic/isoechoic in echotexture; hypoechoic lesions have a higher risk of being malignant [46].
- Predominantly solid and homogeneous in 70% [46].
- Well-defined, haloed in 80% [46].
- Benign lesions have a typeII vascularity, whereas malignant lesions have a type III vascularity [34].

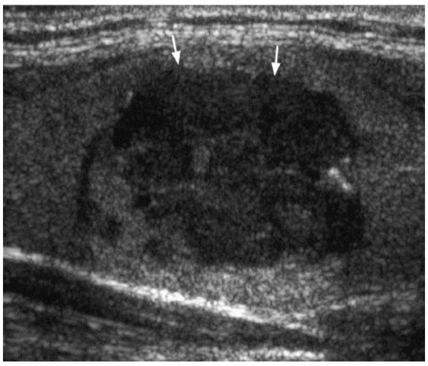


Fig21: Longitudinal grey scale sonogram shows a nill-defined heterogeneous thyroid nodule (arrows). The hypoechoic nature of the follicular lesion raises the suspicion of follicular carcinoma which was confirmed on subsequent thyroidectomy.

Ultrasound, in most cases, cannot accurately distinguish a benign from malignant follicular lesion. The suspicion of malignancy is raised if the nodule is ill-defined, hypoechoic, has a thick irregular capsule and chaotic intranodular vascularity. The only reliable signs of malignancy on ultrasound include frank vascular invasion to adjacent vessels (such as internal jugular vein and common carotid artery) and extra capsular spread.

Thyroid metastases

Metastases to the thyroid gland is infrequent; the incidence in patients with known primary is 2%–17% [47]. Metastases to the thyroid are due to haematogenous spread, most commonly from primary melanoma, breast carcinoma, renal cell carcinoma, lung carcinoma and colonic carcinoma.

Ultrasound features of thyroid metastases include [47]:

- Homogeneous, hypoechoic mass.
- Well-defined margins.
- Predominantly in the lower pole.
- Heterogeneous echopattern when the gland is diffusely involved.
- Multiple, hypoechoic solid, thyroid nodules.
- Chaotic intramodular vascularity.

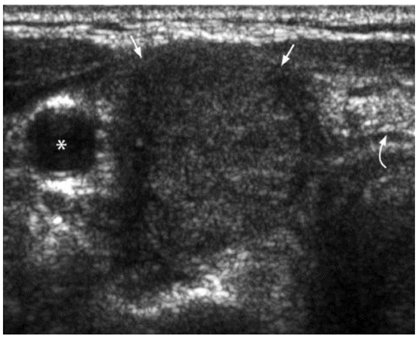


Fig22: Transverse grey scale sonogram in a patient with known breast carcinoma shows a well-defined, solid, homogeneous hypoechoic mass (arrows) occupying the right lobe of thyroid. FNAC confirmed a metastatic carcinoma.

Lymphoma

Lymphoma accounts for 1–3% of all thyroid malignancies. An antecedent history of Hashimoto's thyroiditis is commonly present [26,35]. Thyroid involvement is more commonly seen in non-Hodgkin's lymphoma than in Hodgkin's disease. The typical clinical presentation is an elderly female witha rapidly enlarging neck mass. Thyroid involvement may be focal or diffuse, extra thyroidspread and vascular invasion are seen in 50%–60% and 25%, respectively [48,49].

Ultrasound features of lymphoma of thyroid gland include:

- Focal thyroid involvement may be seen as a well-defined nodule with pseudocystic appearance or heterogeneous appearance.
- Diffuse involvement may result in heterogeneous echopattern or simple enlargement of the gland with normal echopattern.
- Associated round, hypoechoic, reticulated lymphomatous nodes in the neck.
- Background of previous Hashimoto's thyroiditis in the formof echogenic fibrous strands within the thyroid gland is often seen.

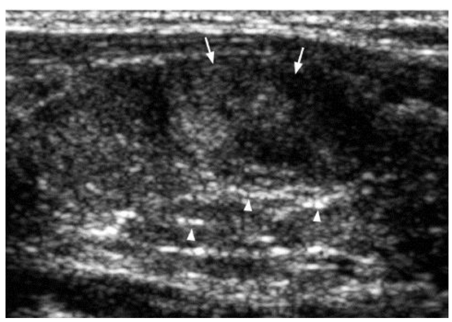


Fig23: Longitudinal grey scale sonogram shows a nill-defined, solid, hypoechoicnodule (arrows) in the thyroid gland. Thin echogenic lines (arrowheads) in the adjacent thyroid glandular parenchyma indicates background Hashimoto's thyroiditis. Biopsy confirmed non- Hodgkin lymphoma of the thyroid gland.

Chapter two

Methodology

METHODOLOGY

Type of study:

Cohort prospective & retrospective study.

The study population:

All patients with thyroid nodules that had have thyroid U/S and surgery or biopsy or FNAC. With different gender & age groups.

The duration of study:

December 2010 – July 2012.

The study area:

Khartoum state hospitals.

U/S Examination Technique:

All U/S examinations were performed with a 7MHz or above linear-array transducer. The scanning protocol included both transverse and longitudinal real-time imaging of the thyroid nodules. Radiologists performed or supervised the examinations.

The method of data collection:

From patient examination, radiologist report and the biopsy report.

Analysis of Data:

Statistical analysis was performed by using a software package (SPSS for Windows). Each of the US characteristics was analyzed to determine its association with abenign versus amalignant tissue diagnosis. For each reader, the relevant findings were compared with the tissue diagnosis (reference standard) to determine sensitivity, specificity, negative predictive value, and positive predictive value.

Chapter three

Results

Results

The study included 92 patients presented with thyroid nodules that had have U/S examination and had undergone surgery with biopsy or FNAC. 74 patients (80.4%) were females, and 18 patients (19.6%) were males. 2 patients of less than 20 years (2.2%), 12 patients between 20-30 years (13.0%), 13 patients between 31-40 years (14.1%), 24 patients of more than 41-50 years (26.1%), and 41 patients of more than 50 years (44.6%).

U/S Characteristics:

Nodule size of less than 10 mm is found in 30 patients (32.6%), and size of more than 10 mm is found in 62 patients (67.4%). 17 of the nodules less than 10 mm were benign (56.7%), while 13 were found to be malignant (43.3%).33 of the nodules more than 10 mm were benign (53.2%), while 29 werefound to be malignant (46.8%).

A predominantly solid content is found in 78 patients (84.8%), 38 of them were benign (48.7%), while 40 were malignant (51.3%). A predominantly cystic nodule was found in 14 patients (15.2%), 12 of them were benign (85.7%), while just 2 were malignant (14.3%).

64 nodules were found having ovoid to round shape (69.6%), 45 of them were benign (70.3%), while 19 were malignant (29.7%). 17 nodules were having taller than wide shape (18.5%), 14 of them were malignant (82.4%), while 3 were benign (17.6%). And 11 nodules were of irregular shape (12.0%), 9 of them were malignant (81.8%), while 2 were benign (18.2%).

55 of nodules were found to have well defined smooth margins (59.8%), 42 of them were benign (76.4%), while 13 were malignant (23.6%). 25 nodules found to have speculated margins (27.2%), 22 of them were malignant (88.0%), while just 3 were benign (12.0%).12 nodules were found to have ill- defined margins (13.0%), 7 of them were malignant (58.3%), while 5 were benign (41.7%).

54 nodules were found to be hypoechoic (58.7%), 36 of them were malignant (66.7%), while 18 were benign (33.3%). 32 nodules were found isoechoic (34.8%), 28 of them were benign (87.5%), while 4 were malignant (12.5%). 6 nodules were hyperechoic (6.5%), 4 of them were benign (66.7%), while 2 were malignant (33.3%).

20 nodules found to have micro calcification (21.7%), 18 of them were malignant (90.0%), while just 2 were benign (10.0%). 11 nodules found to have macro calcification (12.0%), 7 of them were benign (63.6%), while 4 were malignant (36.4%). 4 nodules were found to have rim calcification (4.3%), 2 benign (50.0%), and 2 malignant (50.0%). 57 nodules showed no calcification (62.0%), 39 of them were benign (68.4%), and 18 weremalignant (31.6%).

39 of nodules showed intra nodular vascularization on color Doppler analysis (42.4%),28 ofthemwere malignant (71.8%), and 11 werebenign (28.2%). 23 nodules showed perinodular vascularization (25.0%), 19 of them were benign (82.6%), and 4 were malignant (17.4%). 30 nodules showed novascularization on Doppler analysis (32.6%), 20 of them were benign (66.7%), and 10 were malignant (33.3%).

56 patients were found to have multinodular goiter (60.9%), 38 of them were benign goiters (67.9%), and 18 were malignant ones (32.1%). 36 patients were found to have solitary nodules (39.1%), 24 of them were malignant (66.7%), and 12 were benign (33.3%).

Both lobes were affected in 55 patients (59.8%), 42 of them were benign (76.4%), and 13 were malignant (23.6%). While just one lobe affected in 37 patients (40.2%), 29 were malignant (78.4%), and 8 were benign (21.6%).

Regional enlarged lymph nodes were found in 16 patients (17.4%), 14 of them were malignant (87.5%), and 2 were benign (12.5%). While no lymph node enlargement seen in 76 patients (82.6%), 48 were benign (63.2%), and 28 were malignant (36.8%).

Statistically significant ($P < 0.05$) findings of malignancy were a taller than wide shape, speculated margins, hypoechogenicity, micro calcification, solitary nodules, presence of enlarged regional lymph nodes, and intranodular vascularization on Doppler analysis.

Statistically significant ($P < 0.05$) findings of benign nodules were isoechogenicity, a round to ovoid shape, a well-defined margin, a cystic content, an absent calcification, multinodularity, and perinodular vascularity.

No statistical significant ($P > 0.05$) difference found for hyperechogenicity, ill-defined margins, solid content, macro & rim calcification, absent vascularization on Doppler analysis, and comet-tail sign.

Colloid nodule was found to be the more frequent benign nodule as 47 nodules out of 50 (94.0%) were found colloid nodule in histopathology, where 2 nodules (4.0%) were inflammatory nodules, and 1 nodule (2.0%) was thyroid cyst.

Follicular carcinoma was found more frequent malignant nodule as 18 nodules out of 42 (42.9%) were found as follicular carcinoma, where 12 nodules (28.6%) were papillary carcinoma, 7 nodules (16.7%) were anaplastic carcinoma, 2 nodules (4.8%) were undifferentiated carcinoma, 1 nodule (2.4%) medullary carcinoma, 1 nodule (2.4%) lymphoma, and 1 nodule (2.4%) metastasis.

Table (1): Age Groups of the study population:

Age	Benign	Malignant	Total
< 20years	2	0	2
20– 30years	10	2	12
31– 40years	11	2	13
41– 50years	18	6	24
>50years	9	32	41
Total	50	42	92

Fig (1): Age Groups of the study population:

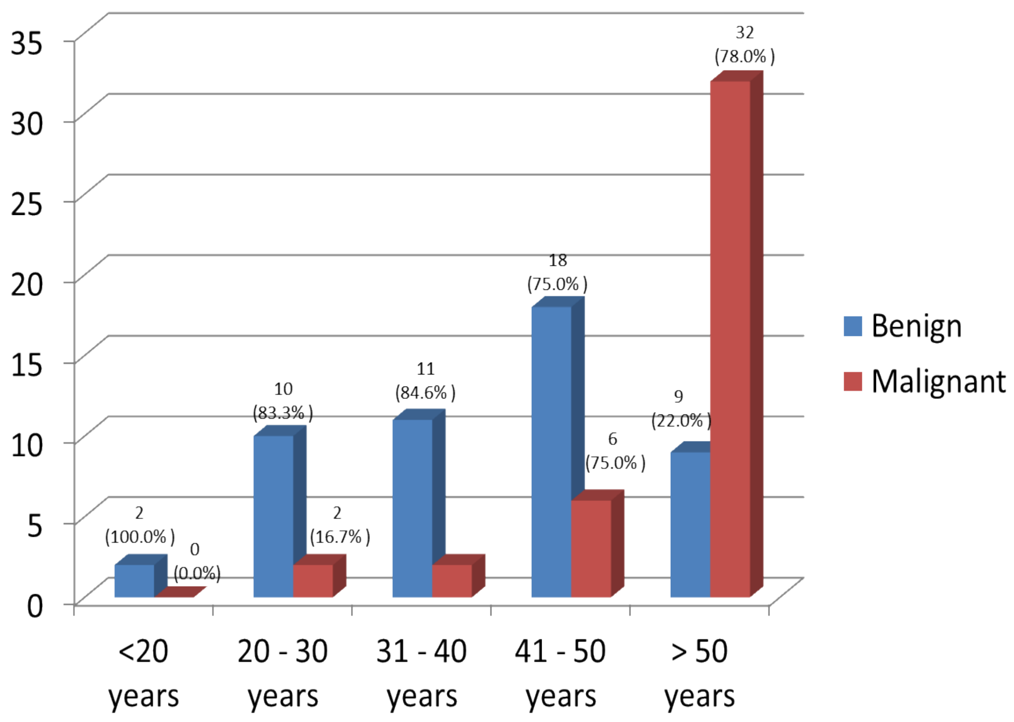


Table (2): Gender of the population:

Gender	Benign	Malignant	Total
Male	9	9	18
Female	41	33	74
Total	50	42	92

Fig (2): Gender of the population:

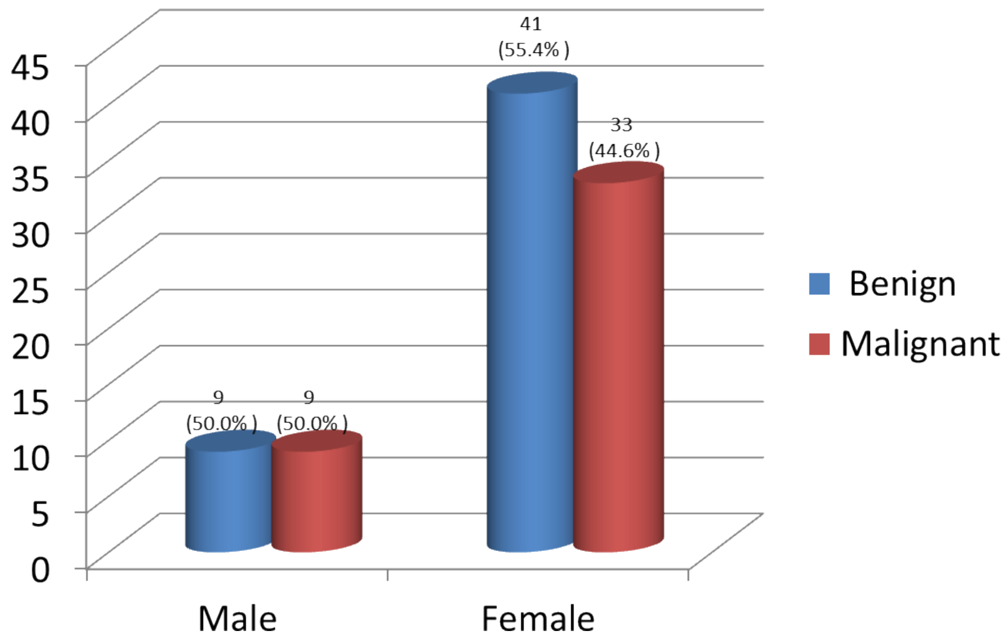


Table (3): The relation between the nodule size & histopathology result:

Nodulesize	Benign	Malignant	Total
<10mm	17	13	30
>10mm	33	29	62
Total	50	42	92

Fig (3): The relation between the nodule size & histopathology result:

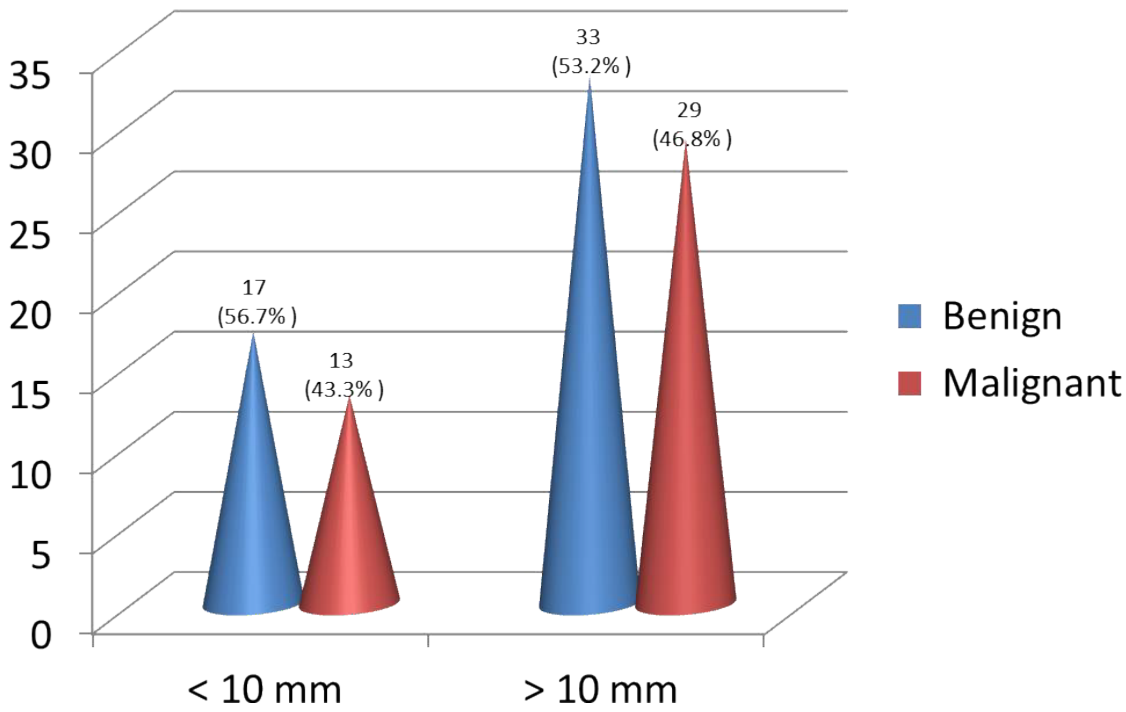


Table (4): The relation between the nodule shape & histopathology result:

Noduleshape	**Benign**	**Malignant**	**Total**
Ovoidto round	45	19	64
Irregular	2	9	11
Tallerthanwide	3	14	17
Total	50	42	92

Fig (4): The relation between the nodule shape & histopathology result:

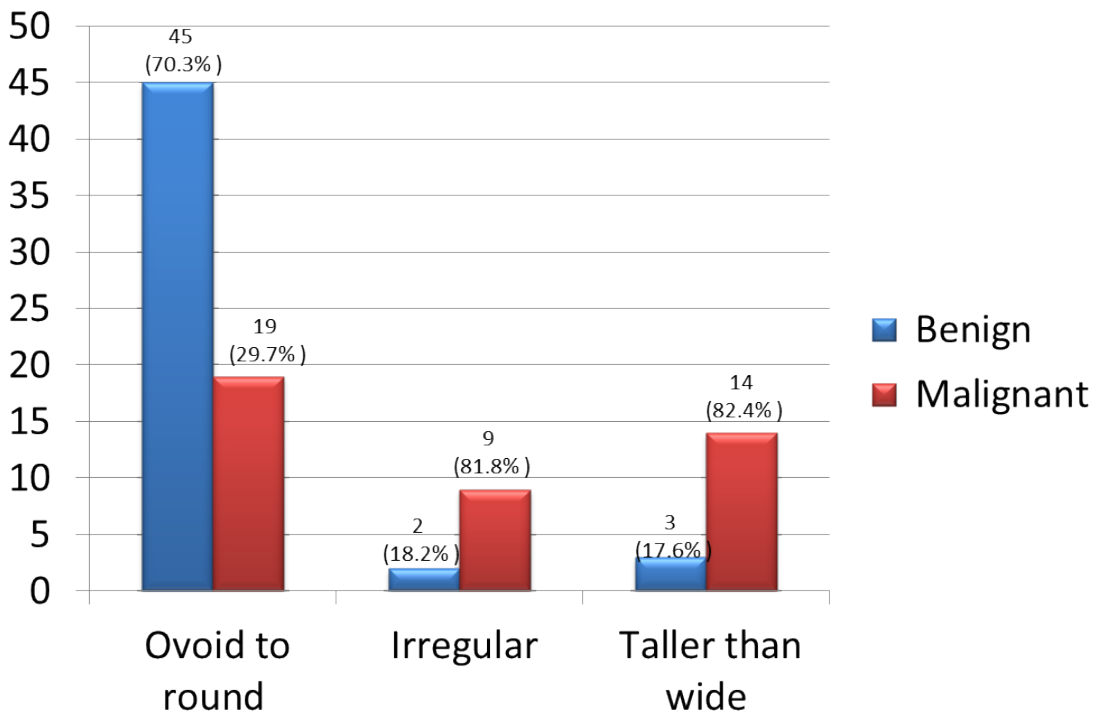


Table (5): The relation between the nodule margins & histopathology result:

Nodulemargin	**Benign**	**Malignant**	**Total**
Welldefinedsmooth	42	13	55
Welldefinedspeculated	3	22	25
Illdefined	5	7	12
Total	50	42	92

Fig (5): The relation between the nodule margins & histopathology result:

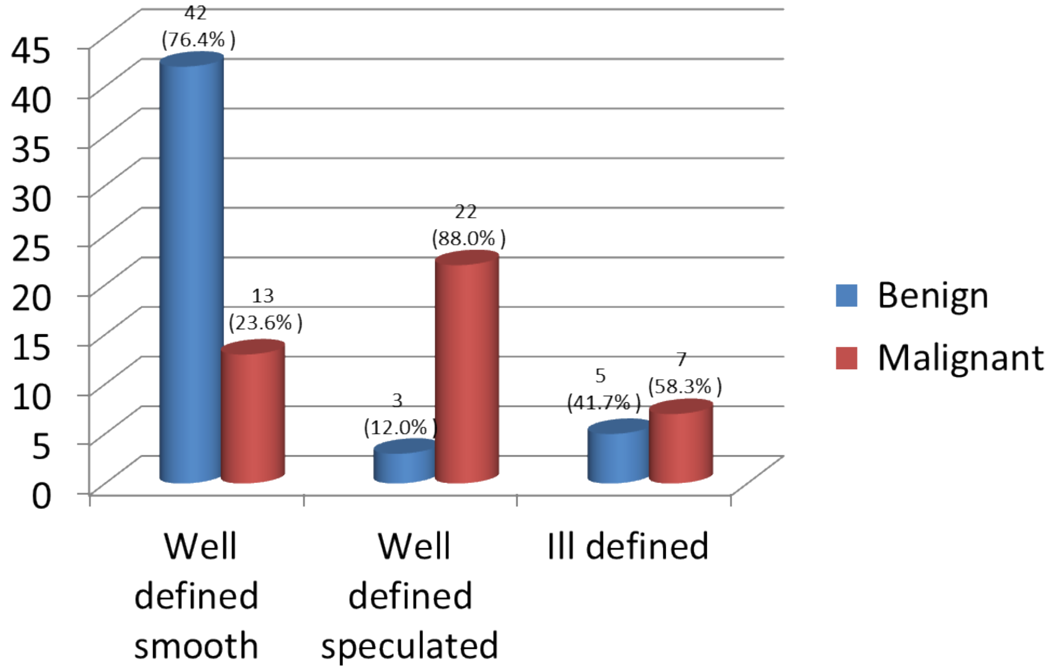


Table (6): The relation between nodule echogenicity & histopathology result:

Echogenicity	Benign	Malignant	Total
Hypoechoic	18	36	54
Isoechoic	28	4	32
Hyperechoic	4	2	6
Total	**50**	**42**	**92**

Fig (6): The relation between nodule echogenicity & histopathology result:

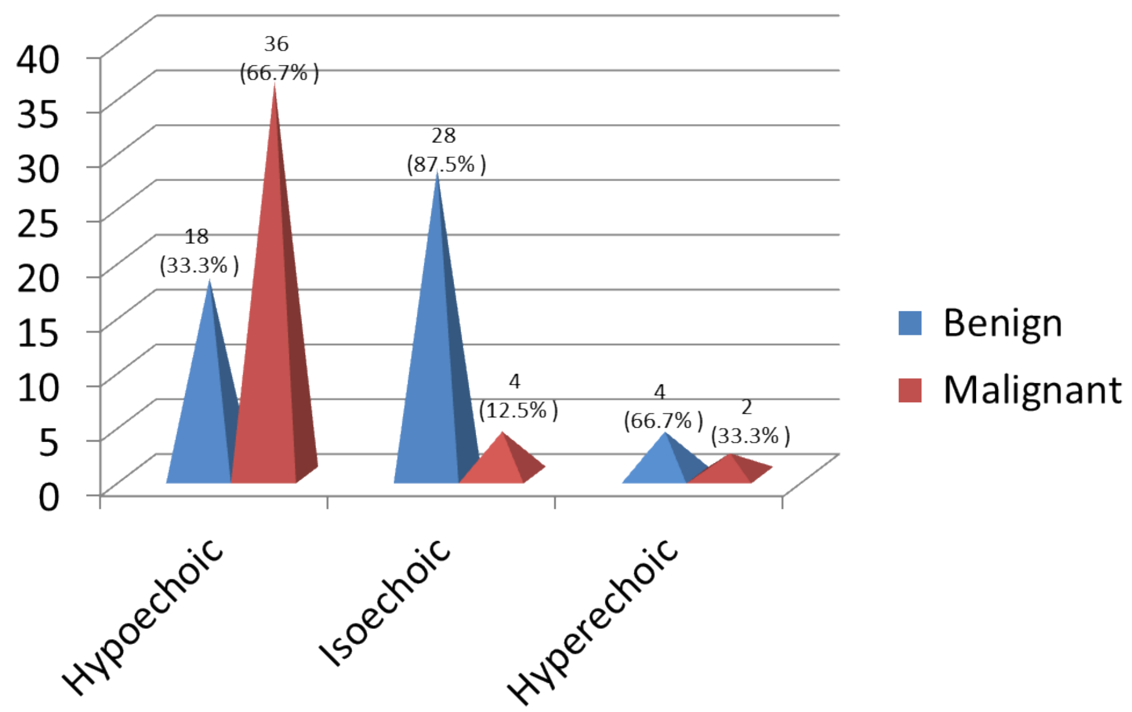


Table (7): The relation between the nodule content & histopathology result:

content	Benign	Malignant	Total
Predominantlysolid	38	40	78
Predominantlycystic	12	2	14
Total	**50**	**42**	**92**

Fig (7): The relation between the nodule content & histopathology result:

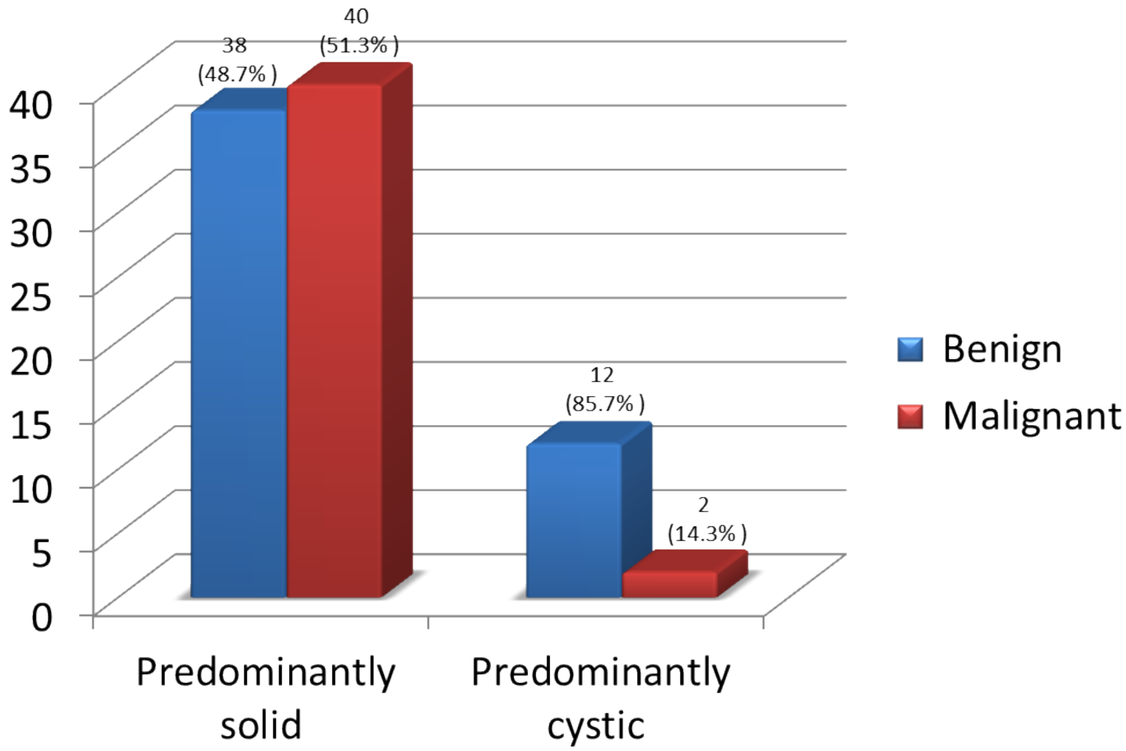


Table (8): The relation between type of calcification of the nodule & histopathology result:

Type of calcification	Benign	Malignant	Total
Absent	39	18	57
Rimcalcification	2	2	4
Micro calcification	2	18	20
Macro calcification	7	4	11
Total	**50**	**42**	**92**

Fig (8): The relation between type of calcification of the nodule & histopathology result:

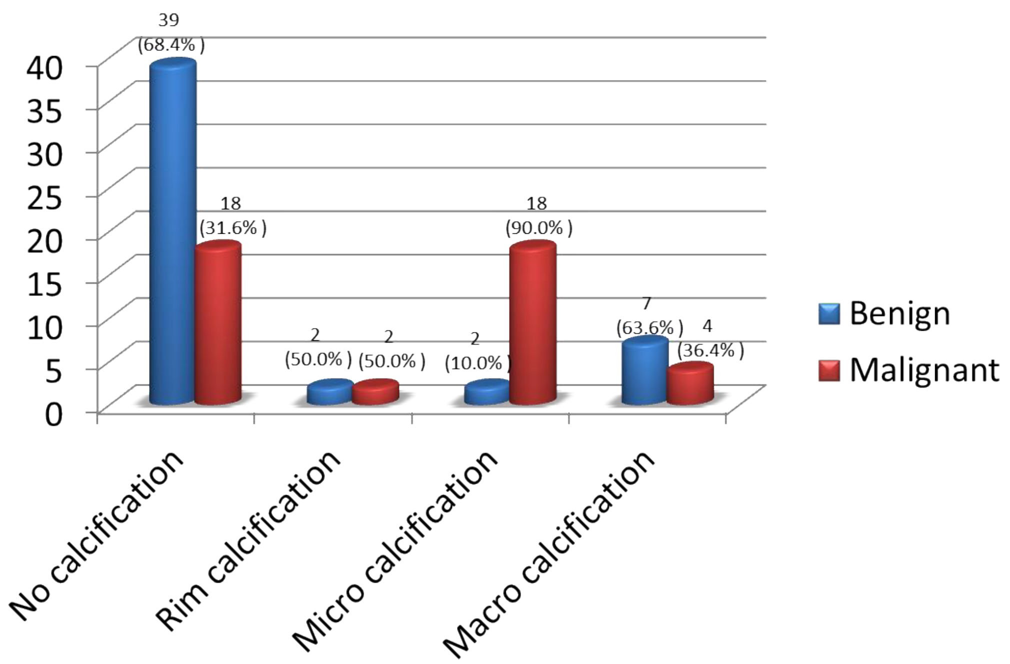


Table (9): The relation between nodule Doppler flow pattern & histopathology result:

Vascularity	Benign	Malignant	Total
Absent	20	10	30
Perinodular	19	4	23
Intranodular	11	28	39
Total	**50**	**42**	**92**

Fig (9): The relation between nodule Doppler flow pattern & histopathology result:

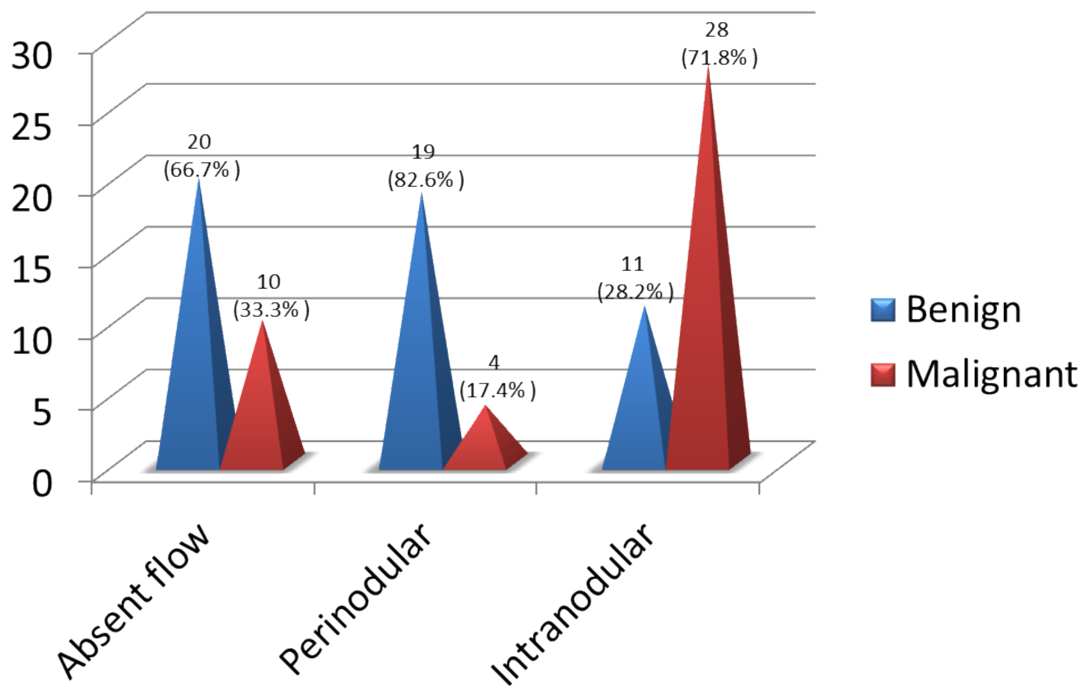


Table (10): The relation between Comet-tail sign & histopathology result:

Comet-tail sign	Benign	Malignant	Total
Yes	4	0	4
No	46	42	88
Total	**50**	**42**	**92**

Fig (10): The relation between Comet-tail sign & histopathology result:

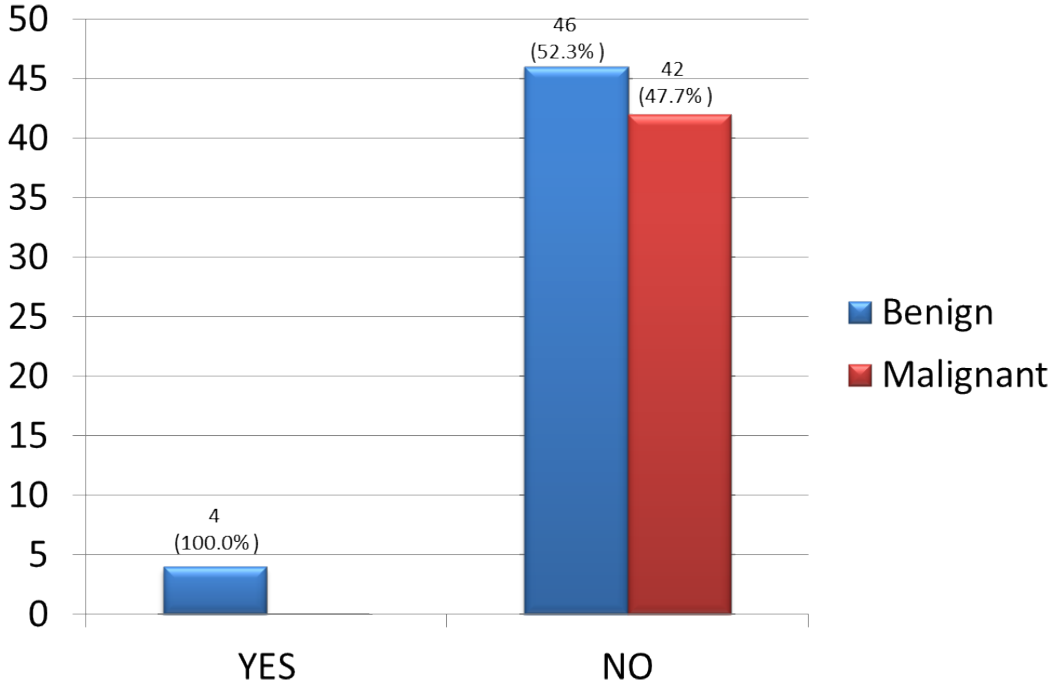


Table (11): The relation between multinodularity & histopathology result:

Multinodularity	**Benign**	**Malignant**	**Total**
Multinodular	38	18	56
Solitarynodule	12	24	36
Total	**50**	**42**	**92**

Fig (11): The relation between multinodularity & histopathology result:

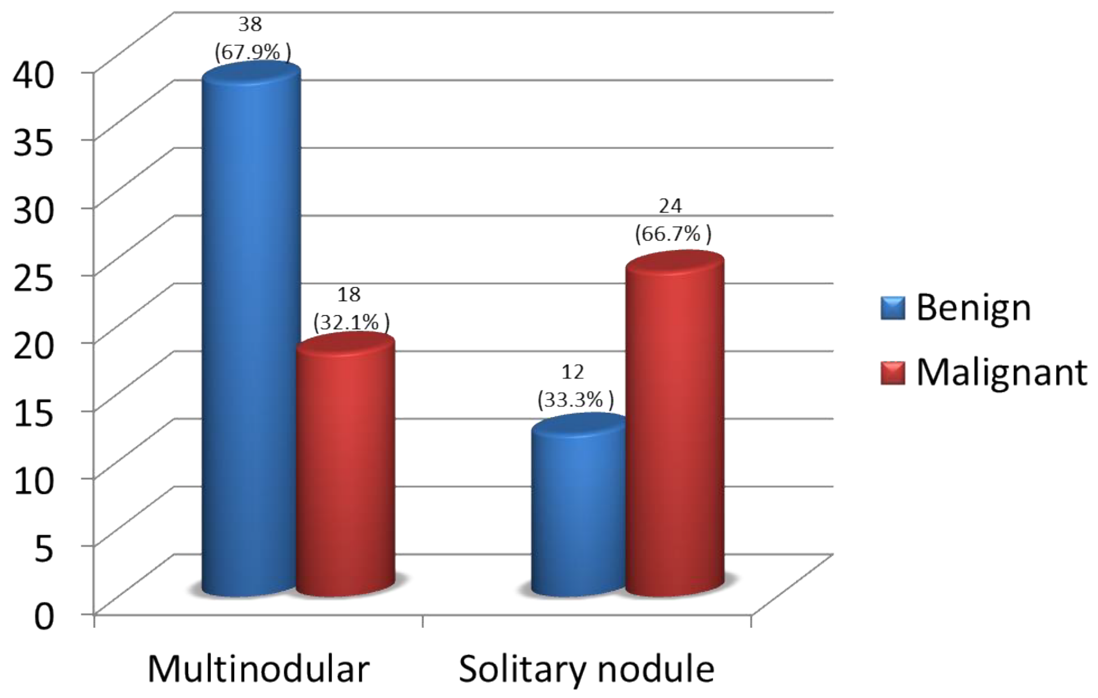


Table (12): The relation between presence of lymphadenopathy & histopathology results:

Regional lymphadenopathy	Benign	Malignant	Total
YES	2	14	16
NO	48	28	76
Total	**50**	**42**	**92**

Fig (12): The relation between presence of lymphadenopathy & histopathology results:

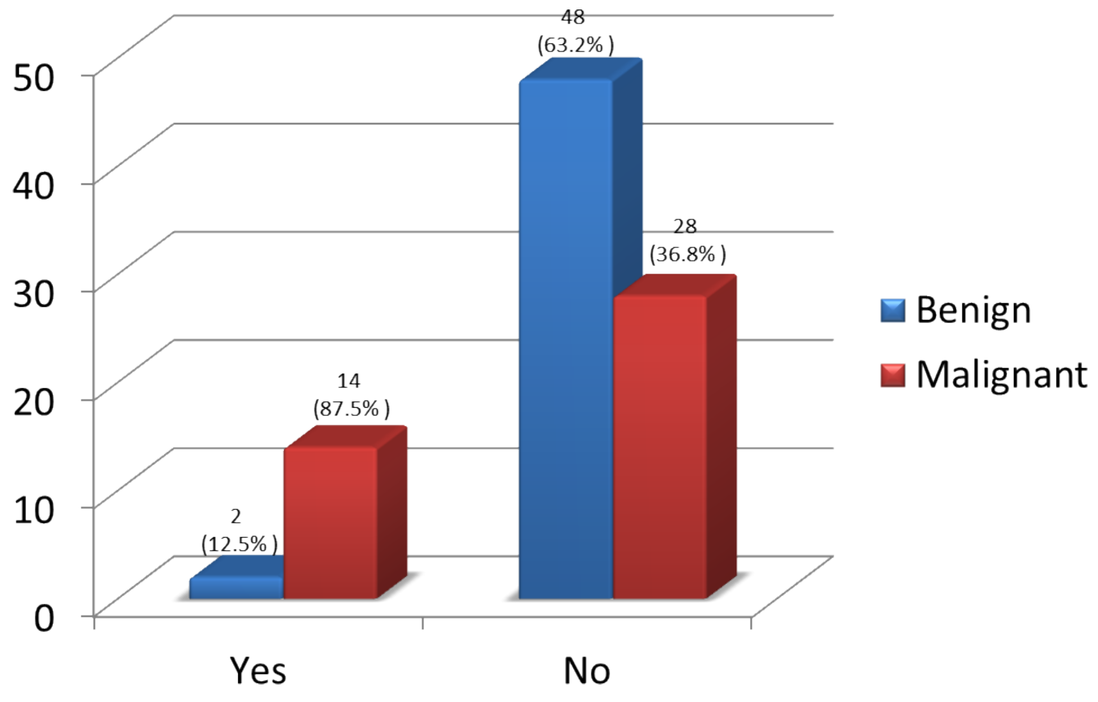


Table (13): Types of benign thyroid nodules according to histopathology results:

Histopathology	**Frequency**	**Percentage**
Colloid nodule	47	94.0%
Inflammatory nodule	2	4.0%
Thyroidcyst	1	2.0%
Total	50	100.0%

Fig (14): Types of benign thyroid nodules according to histopathology results:

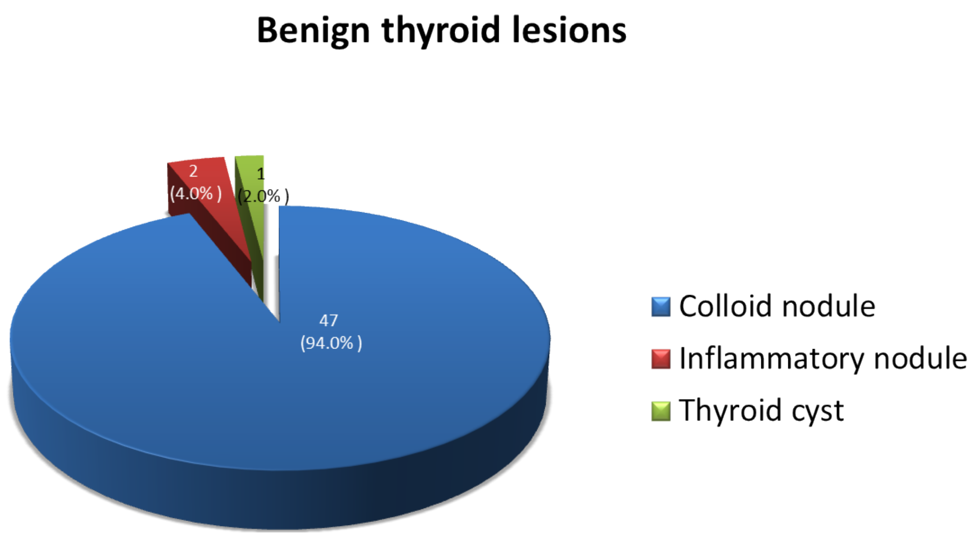
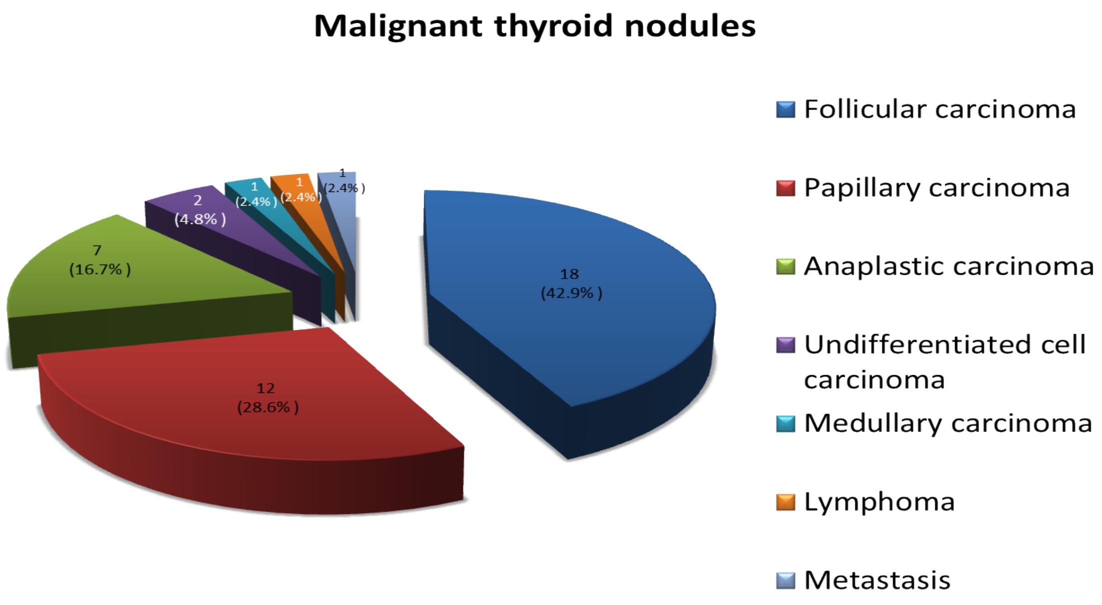


Table (14): Types of malignant thyroid nodules according to histopathology results:

Histopathology	Frequency	Percentage
Follicular carcinoma	18	42.9%
Papillary carcinoma	12	28.6%
Anaplastic carcinoma	7	16.7%
Undifferentiated cell carcinoma	2	4.8%
Medullary carcinoma	1	2.4%
Lymphoma	1	2.4%
Metastasis	1	2.4%
Total	42	100.0%

Fig (14): Types of malignant thyroid nodules according to histopathology results:



Chapter four

DISCUSSION

Conclusion

Recommendations

REFERENCES

APPENDIX

DISCUSSION

The study included 92 patients, 50 of them were having benign thyroid nodules, and 42 were having malignant nodules.

Traditionally, a predominantly solid component regarded as being suggestive of malignant nodule rather than benign nodule. In this study, most of the benign nodules as well as the malignant nodules were predominantly solid. Therefore, a predominantly solid component alone can't be a useful criterion for the differentiation of malignant from benign nodules. The study showed that a predominantly cystic component is a benign feature (sensitivity ***24.0%***, specificity ***95.2%***, positive predictive value ***85.7%***, and negative predictive value ***51.3%***).

The study supports the suggestion that a taller than wide shape is a veryspecific for differentiating malignant thyroid nodules from benign ones (sensitivity ***33.3%***, specificity ***94.0%***, positive predictive value ***82.4%***, and negative predictive value ***62.7%***), the feature that reflects the fact that malignant nodules grow across tissue planes, while benign nodules grow parallel to normal tissue planes. Also, irregular shape was found as a malignant feature (sensitivity ***21.4%***, specificity ***96.0%***, positive predictive value ***81.8%***, and negative predictive value ***59.3%***).

Also, the study supports that round to ovoid shape as a differentiating featureof benign nodules from malignant ones despite that 45.2% of malignant nodules were found to have this feature (sensitivity ***90.0%***, specificity ***54.8%***, positive predictive value ***70.3%***, and negative predictive value ***82.1%***).

The nodule margin was categorized into three subtypes: well-defined smooth, speculated, and ill-defined. The findings showed that a speculated margin is suggestive of malignancy (sensitivity ***52.4%***, specificity ***94.0%***, positive predictive value ***88.0%***, and negative predictive value ***70.1%***), while a well- defined smooth margin is a benign feature although 31.0% of malignant nodules showed a well-defined margin (sensitivity ***84.0%***, specificity ***69.0%***, positive predictive value ***76.4%***, and negative predictive value ***78.4%***). An ill- defined margin was found in both benign and malignant nodules and showed no statistical significance in differentiating them.

Hypoechogenicity was found as a malignant feature, despite that 36.0% of benign nodules were hypoechoic (sensitivity ***85.7%***, specificity ***64.0%***, positive predictive value ***66.7%***, and negative predictive value ***84.2%***), while isoechogenicity was found as a benign feature (sensitivity ***56.0%***, specificity ***90.5%***, positive predictive value ***87.5%***, and negative predictivevalue ***63.3%***).

Hyperechogenicity was found in both benign and malignant nodules and has no statistical significance in differentiation between them.

Presence of microcalcification was found as a malignant feature (sensitivity ***42.9%***, specificity ***96.0%***, positive predictive value ***90.0%***, and negative predictive value ***66.7%***), while macrocalcification was found in both benign and malignant nodules. Microcalcifications correspond pathologically to calcified psammoma bodies that are typical of papillary cancer, while macrocalcifications are related to fibrosis and degeneration. Absence of calcification was found as a benign feature in this study (sensitivity ***78.0%***, specificity ***57.1%***, positive predictive value ***68.4%***, and negative predictive value ***68.6%***), while the presence of rim calcification was of no statistical significance in differentiation between benign and malignant nodules.

Also although multinodularity is found to be a benign feature (sensitivity ***76.0%***, specificity ***57.1%***, positive predictive value ***67.9%***, and negative predictive value ***66.7%***) and solitary nodule is found to be a malignant feature (sensitivity ***57.1%***, specificity ***76.0%***, positive predictive value ***66.7%***, and negative predictive value ***67.9%***), 54.8% of malignant nodules were found as multinodular and 24.0% of benign nodules were solitary nodules, so multinodularity can't be used alone as a differentiation feature between benign and malignant nodules.

The study showed that intranodular vascularization is a malignant feature (sensitivity ***66.7%***, specificity ***78.0%***, positive predictive value ***71.8%***, and negative predictive value ***73.6%***), despite the fact that 22.0% of benign nodules found to have the same feature, while perinodular vascularization was found as a benign feature (sensitivity ***38.0%***, specificity ***90.5%***, positive predictive value ***82.6%***, and negative predictive value ***55.1%***), and thatreflects the fact that growth and progression of malignant tumors are dependent on the available blood supply.

Presence of regional enlarged lymph nodes was found to be of statistical significance of being malignant nodule (sensitivity ***33.3%***, specificity ***96.0%***, positive predictive value ***87.5%***, and negative predictive value ***63.2%***).

Conclusion

The management of a thyroid nodule is multi-disciplinary and involves head and neck surgeons, radiologists and pathologists.

U/S features (shape, margins, echogenicity, presence of calcification, type of vascularization, multinodularity& presence of regional lymphadenopathy) were found to be helpful in discrimination of malignant from benign nodules specially when more than one feature are present.

A study in the same subject was done in South Korea by the Thyroid Study Group, Korean Society of Neuro – and Head & Neck Radiology from January 2003 to June 2003 & published in RSNA (Radiological Society of North America) in 2008 revealed results that strengthen the results of this study. The study involved 8024 patients and the results showed that taller than wide shape, speculated margins, marked hypoechogenicity and micro & macrocalcification are U/S features of malignant thyroid nodules, where benign features are isoechogenicity & spongiform appearance.

Another study was published in 2006 in QJM (An International Journal of Medicine: Oxford Journals), the studywas done in the Department of Medical and Surgical Sciences, Internal Medicine and Endocrinology Unit, University of Brescia, Brescia, Italy. The study involved 5198 patients from January1991 to September 2004 and the result showed that microcalcifications, ill-defined margins, solid hypoechoic appearance &intranodular vascular pattern are U/Sfeatures thatfoundto be significantly more frequent in malignant than in benign nodules.

This study and the studies mentioned above showed that no single parameter satisfactorily identifies a subset of patients to be electively investigated by FNAC, although several may be useful in this regard. In this study as mentioned two or more parameters are needed to discriminate malignant from benign thyroid nodule by U/S, and the more frequent malignant patterns were found in combination of solid hypoechoic nodule with calcification (micro or macrocalcification). Where the most frequent benign patterns were cystic nodule with or without internal echoes (comet-tail).

Recommendations

1- Further research on this subject should be encouraged to confirm the role of sonography for differentiation between benign and malignant thyroid nodules.

2- Ultrasound is an operator-dependent examination technique, and a weakness of this investigation is the single-reader study design. So more prospective studies are needed to investigate the general applicability of ultrasonographic (US) features in differentiating benign from malignant thyroid nodules.

3- Radiologists must be familiar with the various signs on ultrasound that help to distinguish benign from malignant thyroid nodules and the typical appearance of common thyroid cancer.

4- The evaluation of thyroid nodules by ultrasound should be regarded in making of clinical decision specially in non-palpable nodules.

5- Ultrasound provides a safe tool for disease surveillance in patients with thyroid cancer after treatment.

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Appendix

Benign Vs Malignant THYROID NODULES: U/S differentiation Data sheet

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Personaldata:

Patient No. (   )   **Age:** (   ) Yrs

Gender: Male (   )   Female (   )   **Residence:** ……………

U/S Findings:

1- ***Size:***

< 10mm (   )   > 10mm (   )

2- **Shape:**

Ovoid to round (   )   Taller than wide (   )   Irregular (   )

3- **Margins:**

Well defined smooth (   )   Well defined speculated (   )   ill defined (   )

*4- **Echogenicity:***

Hypoechoic (   )   Isoechoic (   )   Hyperechoic (   )

5- **Content:**

Predominantly solid (   )   Predominantly cystic (   )

6- **Calcification:**

Microcalcification (   )   Macrocalcification (   )   Rim (   )   Absent (   )

*7-**Multinodularity:***

Solitary nodule (   )   Multinodular (   )

8- **Colour flow pattern:**

Absent (   )   Perinodular (   )   Intranodular (   )

9- ***Comet-tail sign:***

Yes   (   )   No (   )

10- ***Lobes affected:***

One lobe (   )   Both lobes   (   )

11- *Effect on adjacent structures:*

Yes ( ) No ( )

In case of yes, which structure: ………………………………….

12- *Regional lymph nodes:*

Yes ( ) No ( )

Histopathology:

Benign:

- Colloidnodule ( )
- Follicularadenoma ( )
- Thyroidcyst ( )
- Inflammatory nodule ( )

Malignant:

- Papillary carcinoma ( )
- Medullary carcinoma ( )
- Follicular carcinoma ( )
- Anaplastic carcinoma ( )
- Metastasis ( )
- Lymphoma ( )