The Research of Medical Science Review

Received: 03 December, 2024
Accepted: 03 January, 2025
Published: 10 January, 2025

ISSN: 3007-1208 | 3007-1216
Volume 3, Issue 1, 2025

ASSESSING THE CLINICAL UTILITY OF SONOELASTOGRAPHY FOR DIFFERENTIATING MALIGNANT FROM BENIGN THYROID NODULES: CORRELATION WITH HISTOPATHOLOGICAL FINDINGS IN PATIENTS WITH SUSPICIOUS ULTRASOUND FEATURES AT A TERTIARY CARE CENTER

Kamila Mariam Iftikhar[*1], Uzma Bukhari[2], Anum Khalid[3], Syed Muhammad Faiq[4], Soha[5], Rashmeen[6], Rija[7], Fariya[8]

*[*1]Lecturer, Department of Medical Technology, Dow University of Health Sciences (DUHS) Karachi Pakistan.*
[2]Professor, Department of Pathology, Dow International Medical College, Dow University of Health Sciences(DUHS), Karachi Pakistan.
[3,4]Department of Radiology, Sind Institute of Urology and Transplant (SIUT) Karachi Pakistan
[5,6,7,8]Student, Department of Medical Technology, Dow University of Health Sciences (DUHS) Karachi Pakistan

ABSTRACT

AIMS:
The aim is to evaluate sonoelastography's efficacy in diagnosing malignant thyroid nodules in patients with suspicious lesions detected during thyroid ultrasonography at a Karachi tertiary care hospital, using histology as the gold standard.

MATERIAL AND METHODS:
All patients who visited SIUT in Karachi and fulfilled the incorporation requirements were incorporated into the research. Following an explanation of the process, hazards, and advantages of the study, informed consent was obtained. Nodules scoring higher than 4 on sonoelastography were considered malignant. Every piece of information was electronically captured in the given form and used for study.

RESULTS
Mean ± SD of age was 37.7±7.2 years. In distribution of gender,110 patients (63.2%) were female, while 36.8% of the patients were male. Using histopathology as the gold standard, the diagnostic accuracy of sonoelastography was shown to be 70.69% a fatal thyroid nodule can be detected with a sensitivity of 84.78%, specificity of 57.40%, PPV of 46.99%, and NPV of 92.31%.

CONCLUSION
Histopathology is still vital in all cases of malignant thyroid nodules. On the other hand, sonoelastography proved to be more useful in evaluating thyroid nodules than histology.

Keywords: *Diagnostic Accuracy, Sonoelastography, Thyroid Nodule, Ultrasound.*

INTRODUCTION

Thyroid malignancy may present either as a solitary cold nodule, as a multinodular goiter (MNG), or as an enlarged cervical lymph node [1]. About 7% adult populations have palpable thyroid nodules. Women are affected more than men especially with advancing age. Most of these thyroid lesions are benign with few malignant cases. About 67% of thyroid nodules are smaller than 15 mm in size [2]. While it was once believed that nodes less than 15 mm were benign and did not require additional research, a number of recent

studies have refuted this theory and demonstrated that small nodules can be malignant, necessitating additional research [3]. It is generally acknowledged that the best techniques for comparing benign and malignant nodules are sonography and ultrasound-guided FNA cytology. [4]. Thus, the primary challenge in thyroid nodule management is separating malignant from benign nodules in the clinic [5]. Histological analyses reveal that between 5 and 10% of the palpable nodules are cancerous [6]. During the same period, if a nodule feels stiffer than usual during a physical examination, it can serve as a direct indication of malignancy. [7]. While ultrasound is a valuable method for diagnosing thyroid nodules, it is not highly accurate in identifying benign from malignant tumors. [8]. Based on the ultrasound characteristics of the nodules, such as small areas of calcification, irregular edges, reduced echogenicity, presence of blood vessels within the nodule, and indistinct boundaries, Ultrasonography's sensitivity and specificity in diagnosing Cancerous nodules ranged from 55% to 95% and 52% to 81%, respectively. [9-10]. The fine-needle aspiration (FNA) biopsy approach is still widely used for finding malignant nodules., although its accuracy varies significantly, with intensity varying from 54% to 90% and perfection from 60% to 98%. [11-12].
Elastography can get over the drawbacks of traditional detection methods and has become a viable method for thyroid nodule diagnosis in the future. Elastography uses the tissue's elasticity or stiffness to distinguish between non-cancerous and malignant nodules. [13]. Because of its anterior and superficial placement, the thyroid gland is in the best possible position for an elastographic assessment. And can be readily compressed by a US probe against underlying anatomic structures. Pre- and post-compression ultrasonic signals are utilized to assess the strain or tissue deformation brought on by compression. [14]. It is hypothesized that tumor thyroid nodules have a substantially higher elastic modulus than innocuous and normal thyroid nodules. Thyroid tissue based on the principles of sonoelastography. This gives the idea for identifying the type of nodules utilizing USE. [15]. numerous varied sonoelastography ratings are applied, depending on variation in color or a numerical estimation of the degree of elasticity. The most often used grading system is Rago's, which uses a color-coded scale of 1 to 5 to assess thyroid nodules qualitatively. Green indicates a benign nodule, whereas blue indicates a cancerous one. [16]. According to Afifi ET AL, 42% of nodules were malignant [6]. Ghajarzadeh et al. used sonoelastography to assess a single thyroid nodule was screened for any signs of a cancerous thyroid nodule identified 66.7% specificity and 86% sensitivity [16].

RATIONALE

Since there are little local data available, the goal of this study is to establish the clarity of prognosis of sonoelastography in the diagnosis of malignant thyroid nodules, with histology serving as the gold standard. A recently developed ultrasonic technique called sonoelastography measures how much tissue is distorted in reaction to an external force. In addition to aiding in the early diagnosis of malignant nodule, this technology can evaluate tissue stiffness and provide a qualitative assessment of the target tissue in addition to standard thyroid ultrasound. Hence avoiding the needless FNAC of patients with worrisome nodules and offering a more economical method of screening individuals at risk of cancer.

THYROID NODULES

Thyroid nodules are typical objects that are often found in clinical practice, either by chance during different imaging methods or during physical examinations. Their propensity for malignancy is the main reason they are clinically significant. Because of this, it is crucial to begin the evaluation with a comprehensive examination that delves into the patient's medical history and includes a thorough physical assessment, specifically targeting any signs or indications of potential malignancy. Levels of serum a hormone called (TSH) and thyroid function using ultrasound (US) two important components of thyroid nodule evaluation: the functionality of the node and the presence of traits that suggest the presence of cancer, therefore. The most exact and dependable biopsy technique is fine-needle aspiration (FNA). A method for diagnosing cancer and identifying patients who are candidates for surgery. When performed with the use of ultrasound imaging. The evaluation of cells from FNA biopsies will fall into an unknown category in roughly [17]. The preoperative diagnosis of ambiguous thyroid nodules has improved recently with using gene mutation panels and molecular markers in combination with cytology diagnosis. Reducing the number of needless operations.

Other methods for assessing the possibility for malignancy in thyroid nodules that are still being studied are 18FDG-PET scanning, a technique that utilizes 18F-fluorodeoxyglucose positron emission tomography, is employed for medical purposes. And elastography. A method for the initial assessment and treatment of cysts, glands with multiple nodules, nodules that are found by chance, single nodules, and functioning nodules is covered. When necessary, therapeutic approaches for benign nodules may involve radioiodine or surgery. (131-I) therapy, or cutaneous ethanol injection (PEI) if required. Levothyroxine (T4) use as reducing therapy is still a subject of controversy and debate. And is typically not encouraged. With the exception of the contraindication to radionuclide scanning, Assessment of pregnancy-related thyroid nodules is essentially the same as for patients who are not pregnant. In the majority of cases, thyroid cancer during pregnancy can be effectively treated through a thyroidectomy after the baby is born. However, if the cancer displays aggressive characteristics, it is advisable to schedule the surgery during the second trimester for optimal outcomes. [17].

CLINICAL IMPORTANCE, DEFINITION, AND EPIDEMIOLOGY

Women and older people are more likely to develop thyroid nodules.

The goal of thyroid nodule examination is to identify nodules that need to be surgically removed or are cancerous. The American Thyroid Association (ATA) claims that [17], Nodules, or tumors, are distinctive growths inside the thyroid gland which seem different from nearby tissue on medical scans. They can be felt on a regular checkup on the body. Alternatively, various imaging tests such as 18FDG-PET scans, CT scans, MRI scans, and carotid duplex ultrasonography can be used. Can be utilized to locate them. Known as "thyroid incidentalomas," the latter items typically don't match up with detectable thyroid tumors. On the other hand, medical professionals may detect palpable thyroid lesions that are not classified as thyroid nodules because they do not match specific radiological structures. [18].

Thyroid nodules are prevalent; the manner of identification greatly influences how often they are. When using high-resolution US techniques, it is possible to detect Nodules can be found in a significant portion of the adult population, ranging from 20% to 76%, compared to the predicted prevalence of 4% to 7% by palpation alone. Between 50% and 65% of the frequencies reported by the US align with the prevalence found during autopsy and surgery. [19].

In the United States, it is estimated that about 0.1% of people develop thyroid nodules each year. This means that over the course of a person's lifetime, there is a 10% probability of developing this condition. [20] The number of thyroid nodules found is twice as high in women compared to men. As age increases and iodine consumption decreases, the frequency of these nodules also increases. The hormonal effects of progesterone and estrogen, which are related to pregnancy and having multiple children, may explain the gender difference. If exposed to ionizing radiation during childhood or at work, thyroid nodules will grow at a rate of 2% per year and reach their highest incidence in 15 to 25 years. [21].

For a number of reasons, thyroid nodules are clinically significant. They are mostly significant because thyroid cancer must be ruled out, but they may also result in thyroid malfunction and, in rare cases, compressive symptoms. When thyroid nodules are examined the recorded occurrence of cancer through biopsy varies from 4.0% to 6.5% and is generally unrelated to the size of the nodule. [22]. In spite of this, papillary micro carcinomas (less than 1 cm) that are unintentionally discovered during surgery are far more prevalent (up to 36%). However, given their largely benign nature, it is debatable whether or not diagnosing and treating these entities improves survival. Crucially, thyroid nodules found by accident during 18FDG-PET imaging have a low occurrence (1%–2%), but a significant risk of malignancy (up to 27%), therefore they need to be evaluated right away. [23].

A PHYSICAL EXAMINATION AND HISTORY

The goal of the physical examination and history should be to find characteristics that are especially suggestive of cancer.

Numerous conditions, from benign etiologies to malignant cancers that may behave violently or slowly over time, can induce thyroid nodules. As such, it is imperative that clinical examination be focused on the

identification of malignant illness indicators. It is important when taking into regard earlier head and neck radiation therapy, get an extensive medical record and do a thorough physical examination, the appearance of a lump in the neck, the size, position, and characteristics of the thyroid nodule, the presence of swollen lymph nodes in the neck, and any signs of hypothyroidism or hyperthyroidism. [24]. It is crucial to examine instances of thyroid illness in the family. Follicle cells have been related to the two types of hereditary non-medullary thyroid cancer and ancestral medullary thyroid cancer cells. These two uncommon yet significant familial thyroid conditions, MTC and PTC, are associated with the existence of C-cell tumors that generate calcitonin. If a patient's parent or sibling has a past of the illness, their likelihood of developing PTC is amplified by three or six times, respectively. [24]. One probable aspect of Many Hormonal Neoplasia (MEN) IIA is genetic MTC.

IIB (marfanoid habitus, pheochromocytoma, MTC, and mucosal and digestive neurofibromatosis) and IIA (a condition known as, MTC, which is and primary excessive parathyroid hormone), or they may appear as the only component.

In addition to occurring in isolation, Werner syndrome, familial polyposis, Cowden disease, and Carney disorder have all been linked to Follicular cell-derived familial thyroid cancer. Cowden disorder is an autosomal dominant condition caused by a mutation in the PTEN gene which leads to hamartoma neoplasms in the skin, oral mucosa, gastrointestinal tract, central nervous system, and genitourinary system. The most common malignancies connected with the syndrome are thyroid and breast cancer. Skin and cardiac myxomas are characteristic of the Carney complex autosomal dominant disease. Pigmentation spots on the skin caused by a variety of endocrinopathies and cancers with both endocrine and no endocrine origins [24]. Individuals who suffer from Werner syndrome, a condition typified by early aging, and familial polyposis, a disorder mainly linked to carcinoma of the colon, have a reduced risk of developing thyroid cancer. [25].

Male sex, age >70 years, young age (<20 years), and personal backdrop of rays to the scalp and neck area, especially as a kid, are demographic factors linked to an elevated risk of carcinoma in a nodal thyroid sufferer. It counts. Should be aware it signals like coughing, difficulty swallowing, a raspy voice and are not usually caused by thyroid issues, and that a complete workup should be conducted to rule out other, more typical causes involving the digestive and respiratory systems. [26].

The two most widely utilized diagnostic methods for evaluating thyroid nodule cytopathology are fine-needle capillary sampling (FNC) and FNA. The Bethesda classification, which divides cytologic results into six main categories and indicates varying post-diagnostic evaluation and management, is advised by the National Cancer Institute [27].

The Research of Medical Science Review

According to the Bethesda method, the following diagnostic categories are used to report thyroid cytopathology [27]:

1. Non-diagnostic: Indicates an insufficient sample with a low concentration of cells called proliferative
2. Normal harmless thyroid cells exhibiting multinodular goiters or adenomatous nodules; common conditions include subacute granulomatous thyroiditis, Hashimoto thyroiditis, and adenomatous nodules.
3. Atypia of proposed for lesions that do not appear to be benign: Unknown significance (AUS) or filamentous lesion of unknown significance (FLUS). AUS shows strong oncocytic changes and lesions. With nuclear atypia, however not enough for these lesions to be considered Hürthle cell neoplasms. FLUS combines macro follicular and micro follicular patterns. Micro follicular or cellular adenomas are considered to be follicular neoplasms or to be suspicious for them. Hyperparathyroidism), or they may appear as the only component.

In addition to occurring in isolation, Werner syndrome, familial polyposis, Cowden disease, and Carney disorder have all been linked to follicular cell-derived familial thyroid cancer. Cowden disease is an autosomal dominant illness caused by a mutation in the PTEN gene, which results in hamartoma neoplasms of the skin, oral mucosa, gastrointestinal tract, central nervous system, and genitourinary system. The most common malignancies connected with the syndrome are thyroid and breast cancer. Skin and cardiac myxomas are characteristic of the Carney complex autosomal dominant disease [28].

4. Possible indication of cancer: Encompasses abnormalities exhibiting characteristics of malignancy without conclusive evidence of thyroid cancer.

5. Malignancy: Different types of thyroid cancers exhibit distinct cytological characteristics when observed under a microscope. For instance, papillary tumors are characterized by the presence of large cells with ground-glass cytoplasm, prominent nucleoli, and intranuclear cytoplasmic inclusions. On the other hand, medullary carcinoma is typically identified by dispersed cells with nuclei that are eccentrically displaced, along with somewhat granular cytoplasm that forms a teardrop-like arrangement. Anaplastic cancer, on the other hand, is distinguished by significant pleomorphism, the presence of unusual large cells, and spindle cells. [26-28].

When most patients first arrive, they will have a large palpable lump in the anterior neck, or an incidental lesion, may be discovered during imaging studies for a variety of reasons. The majority of patients with thyroid nodules are euthyroid, with less than 1% developing thyroid illness. Most of thyroid nodules generate absence of symptoms Some individuals experience discomfort or pressure on their necks, especially after there is spontaneous bleeding.[29].

Gland examination is the most straightforward but most inaccurate means of recognizing nodules in the thyroid gland, having a detection rate of 4% to 7% [30]. Examining the body evidence that should raise concerns for neoplasia are vocal fold paralysis, adhesion to surrounding tissues, stiffness when handled, and nodules larger than 4 cm in size. (Which represent for approximately 19% of the risk for malignancy), and the condition known as cervical lymphadenopathy. In rare situations, bodily it may trigger problems during a medical examination. [30]. A single nodule seen on physical examination, cervical lymphadenopathy (more than 1 cm), and vocal fold paralysis have a positive predictive value of nearly 100% for thyroid cancer. [30].

A patient's appropriate social history is crucial and could help identify those who have MEN II condition. They require the proper workup before to surgery since they have an increased risk of pheochromocytomas. Intervention [31].

DIAGNOSTIC STUDIES

Thyroid nodule evaluation can be aided by a variety of diagnostic investigations. Among them are blood indicators like calcitonin and serum thyrotropin (TSH). In order to evaluate thyroid nodules, aspiration with a (FNA) cytology is the primary method Cytology samples can also be utilized to discover genetic markers associated with BRAF mutation thyroid cancer. Furthermore, there may be a role for immunohistochemistry markers including cyclooxygenase 2, galectin-3, and cyclin D2. When evaluating thyroid nodules, ultrasonography is essential, and elastography could be a useful supplement Additional imaging studies.MRI, CT, and 18FDG-PET scans, among others, may be beneficial in some circumstances. The diagnostic workup includes serum markers, fine-needle aspiration cytology (FNA), genetic markers, immunohistochemical markers, and many imaging modalities—ultrasonography is the most prevalent [29-31].

SERUM INDICATORS:

As blood TSH levels rise, thyroid nodule cancer risk rises as well.

Individual with a thyroid nodule must have a TSH test performed as part of their initial workup, since it serves as a guide for ongoing treatment [32].Whereas a low TSH often indicates benignity, a regular or high TSH level may climb. Concerns about a nodule's potential for malignancy. Thus, the following phase in the assessment an individual with a low TSH score would have an iodine-123 (123-I) or pertechnetate imaging scan to identify the presence of an independently functioning nodule. Nonfunctioning or "cold" thyroid nodules in low TSH values in some patients signal cancerous potential’s levels have been linked to advanced-stage thyroid cancer. [32].

THYROID ULTRASONOGRAPHY:

Enables the detection of nodules with concerning appearances for biopsy. Thyroid ultrasound is a crucial method that's frequently utilized to find and assess thyroid nodules. It's a low-cost, noninvasive method that gives information about the size, shape, and thyroid nodule parenchymal alterations. It is now possible to find lesions as small as 2 to 3 mm with brightness- modality US and high-frequency transducers, which begs the question of whether thyroid nodules warrant additional testing in terms of their clinical significance. [34].

Prior research has examined thyroid ultrasound's capacity to distinguish between benign and malignant tumors, hence preventing the needless use of invasive procedures. Consequently, it has been discovered that a number of US characteristics are suggestive of malignant potential. It was shown that distinct risk factors for malignancy were micro calcifications, uneven or micro lobulated edges Hypo echogenicity, taller-than-wide shape, and increased intranodular vascularity. [35]. these suspicious features have a poor sensitivity, reducing their positive predictive value despite their high specificity. It is critical to understand that none of these US features alone can distinguish between benign and malignant tumors; rather, a combination of at least two of them can more effectively identify a subset of lesions that are very likely to turn malignant. Papini et al. shown that thyroid lesions requiring extra cytologic testing can be diagnosed using US characteristics and nodules with a hypoechoic appearance. [36]. A mostly cystic lesion without microcalcifications has a 1.0% chance of being cancerous, whereas a largely A solid lump with tiny calcium deposits has a 31.6% risk of turning malignant. [37].US discoveries such spongiform appearance and isoechogenicity, which are described as aggregations of More than 50% of the nodule having several microcysts is a sign of benignity. [38].

ELASTOGRAPHY:

Elastography is an effective method to deciding whether thyroid nodules are likely to become malignant. Elastography has recently enabled a significant progress in thyroid nodule diagnosis. This dynamic technique analyses tissue hardness as a possible malignancy indicator. This approach has been proven to be exceptionally sensitive (82%-97%) and specific (96%-100%) for the diagnostic evaluation of thyroid nodules, independent of their size or position inside the thyroid gland itself. [39]. It displayed reliability when used in the diagnostic assessment of indeterminate/follicular lesions, although this aspect of its applicability must be validated. Elastography's diagnostic yield is lowered in nodules with calcified shells, cystic lesions, and multinodular goitres with coalescent nodules because proper interpretation requires clearly defined edges. Its use is confined to high-end US tools and is not suitable for identifying follicular cancers. Even if more extensive prospective investigations are needed to determine the precision of this diagnostic approach, it remains an effective tool for selecting nodules for FNA [39].

FNA BIOPSY;

Thyroid FNA biopsy is the most reliable, secure, and cost-effective diagnostic technique for examining thyroid nodules. Because FNA performed under US direction has a lower rate of false-negative and non-diagnostic cytology, it is preferred to the palpation-guided approach. This is especially true for nodules that have a mostly cystic component, are nonpalpable, or are situated deep inside the thyroid bed [40]. The choice to conduct FNA sampling ought to be supported by a risk-stratifying strategy that takes into account the past, US features, as well as nodule dimensions. Only in cases when there are many worrisome US characteristics, extracapsular development, aberrant cervical lymph nodes, or a high-risk history should sub-centimeter nodules be biopsied. Otherwise, solid nodules with a single suspicious sonographic characteristic (microcalcifications, hypoechoic appearance) might be classified with a cutoff size of 1 cm. If a mixed cystic-solid lesion is larger than 1.5 cm, the solid component should be the focus of the biopsy procedure. Lesions that are just cystic or spongiform may be watched or, if they are larger than 2 cm, biopsied due to their low risk of cancer. [41].

CYTOLOGIC DIAGNOSIS:

FNA with an appropriate sample is 95% accurate for diagnosing thyroid cancer. Due to inadequate preparation methods or sampling errors, about 20% of FNA results are non-diagnostic [41]. In these situations, it is advised to perform a second FNA under US supervision and, if possible, to conduct an on-site cytologic evaluation to improve cytologic adequacy. Roughly 7 percent of the nodules will continue to produce inadequate cytologic findings after many biopsies. Surgery is strongly advised in this case for the solid nodules, and as the partially cystic lesions may harbor neoplastic potential, close surveillance or surgery is advised for them. [42].

Diagnostic FNA results are categorized into five categories, based on the most recent Bethesda System for Reporting Thyroid Cytopathology: follicular or Hurthle cell neoplasm, benign (70%), malignant (5%), suggestive for malignancy, and follicular lesions of unclear significance or atypia. 25% of the patients, or the last three cytologic diagnoses, were previously classified as indeterminate lesions. According to forecasts, their odds of having cancer range from 50% to 75%, 20% to 30%, and 5% to 10%, respectively. [43].Among the most prevalent benign lesions are lymphocytic thyroiditis, macrofollicular adenoma, and colloidal nodule. PTC is the most prevalent type of malignant lesion, followed by high-grade metastatic neoplasms, follicular thyroid cancer (FTC), MTC, and anaplastic carcinoma. Uncertain lesions may imply PTC (without definitive diagnostic criteria), lymphoma, Hurthle cell neoplasm, follicular neoplasm, or PTC-follicular variant [44].For malignant and suspicious lesions, surgery, either a lobectomy or a total thyroidectomy, is the preferred course of treatment. Follic lesions follow the same rules, unless a 123-I scan reveals the nodule to be autonomous in the presence of low-normal TSH. Given that FNA produces a high percentage of cystic/solid components in thyroid nodules larger than 3 cm, surgical intervention should be actively considered for diagnostic purposes. [45].

INDETERMINATE CYTOLOGY:

Some FNA biopsies produce cytology findings that cannot definitively determine whether or not there is malignancy present.

Panels consisting of genetic mutations could potentially act as indicators to determine which patients with nodules of uncertain cytology can opt out of surgery without any risks. Currently, the majority of patients whose cytology after FNA biopsy is ambiguous are managed with diagnostic surgery to determine a histological determination. But just 10–40% of these instances will prove to be malignant, meaning that over 60% of surgeries—and the dangers and expenses that go along with them—will be unwarranted [46]. Large prospective studies have demonstrated that the preoperative identification of thyroid nodules can be improved by examining genetic markers connected to thyroid cancer (PTC: BRAF, RAS, RET/PTC; FTC: PAX8/PPARγ1) in the cytology material, especially when paired with cytologic features. For example, in a Korean population, combining FNA cytology with BRAF mutant status increased testing specificity from 36% to 95%. It has been proven that utilizing molecular markers, in patients with indeterminate cytology on FNA samples, a panel of gene mutations increases the likelihood of cancer from 24% to 89% if any mutation is identified, whereas the risk is reduced to 11% in the absence of any mutation [47]. When a molecular panel of gene markers is used in a cost-effectiveness analysis alongside standard cytologic findings to increase the predictive capacity of diagnostic interpretations, encouraging results are produced. In contrast to the surgical method, it is expected to be used in clinical settings in the future. [47].There are now two commercially available assays that allow thyroid cytologic tissues from FNA biopsy to be molecularly tested. Genzyme (Cambridge, MA, USA) markets the VeracyteAfirma Gene Expression Classifier, which assesses the messenger RNA (mRNA) expression levels of 142 genes. When assessed in samples with unclear cytology, it has a 96% negative predictive value, which helps patients with benign lesions avoid needless procedures. [48]. According to Li and colleagues' recent cost-effectiveness research [48], regular use of the gene expression classifier reduces the percentage of benign nodule surgeries from 57% (as is the case with present practice) to 14%. Another commercially available test from Asuragen (Austin, TX, USA) is called miRInform Thyroid. It examines a panel of seven molecular markers that are frequently found in thyroid cancers: BRAF, KRAS, HRAS, NRAS, RET/PTC1, RET/PTC3, PAX8/PPARγ. It is In contrast to Veracyte, this medication is intended to improve the preoperative cytologic diagnosis of ambiguous thyroid nodules by identifying those nodules that are more likely to be malignant. Although clinical validation is still awaiting, the analytical specificity and sensitivity were found to be 99% and 95%, respectively. [49].

Aside from genetic markers, other potentially beneficial procedures include immunohistochemical labeling of cytology specimens and the development of novel serum indicators. Galectin-3 is an immunohistochemical marker that, when used in conjunction with traditional cytomorphological diagnostic procedures, has been shown to improve preoperative diagnosis in ambiguous follicular lesions.Recent study, however, suggests that galectin-3 is a better diagnostic tool for PTC than FTC.Measuring blood TSH

receptor mRNA, which functions as a biomarker of circulating thyroid cancer cellswhich can assist detect whether nodules with unclear cytology are cancerous. TSH receptor mRNA levels exceeding 1 ng/µg were nearly 90% predictive of cancer diagnosis. [50]. An 18FDG-PET scan has a high sensitivity for preoperative detection of thyroid nodules with unclear cytology; nevertheless, in 18FDG-PET-positive nodules, histologic diagnosis is still required to differentiate between benign and malignant origins. However, 18FDG-PET may lower the number of unnecessary thyroidectomies by 39%-46%. [51]. It is inefficient in choosing surgical candidates among people with a cytologic diagnosis of follicular neoplasm because benign and malignant nodules with follicular cytology have similar glucose metabolic activity. [51]

INITIAL EVALUATION OF SINGLE NODULES, FUNCTIONAL NODULES, MULTIFOCAL GLANDS, INCIDENTAL NODULES, AND CYSTS:

A patient with a multinodular thyroid is just as likely to get cancer as someone with a single thyroid nodule. TSH levels, US findings, FNA results, scintigraphy results, and molecular test results can all point in various directions during the examination. Cytology will reveal that most nodules are benign. These nodules can be watched instead of requiring rapid additional diagnostic assessment or therapy. [50-51].

A scintigraphy scan (technetium 99mTc pertechnetate or 123-I) should be performed in individuals with thyroid nodules and serologic evidence of low or subnormal TSH levels to get a more complete picture of nodule functionality. Hyperfunctioning nodules are rarely malignant, hence nodules that appear "hot" on scintigraphy should not be considered for FNA biopsy. [32]. the so-called "cold" or isofunctioning nodules, often referred to as nonfunctioning nodules, should be aspirated for additional assessment because they have a 5% to 15% cancer risk. Radioisotope scanning usually has little utility in evaluating nodular functioning in lesions. Smaller less than 1 centimeter [34]. The results of a US examination will record the quantity of nodules in addition to their size and appearance. Notably, Regardless of how many nodules are present, the risk of the risk of thyroid cancer in people with a multinodular goitre is the same as for those with a single nodule. However, as the The number of nodules increases, whereas the risk of malignancy per nodule decreases. If there are two or more nodules larger than one centimeter, the previously mentioned concerning US characteristics should be used to select which, if any, should undergo a FNA biopsy. If not, the largest nodule must be the target of the biopsy. [17].

First, US assessment should be performed on thyroid incidentalomas found by CT or MRI. Subsequent management should be directed by the sonographic features, as previously stated. On the other hand, incidentalomas identified with 18FDG-PET testing have a significant risk of cancer, hence a US evaluation in addition to a FNA biopsy has to be carried out. [32].

Completely cystic lesions are usually regarded as benign, and additional diagnostic testing is not necessary unless a solid component is present.

TREATMENT FOR BENIGN NODULES:

Nodules causing compressive symptoms, toxic nodular illness, and thyroid cysts are best treated surgically.T4 suppressive therapy is contentious due to the danger of iatrogenic hyperthyroidism, although it may prevent the growth of new nodules.

Most benign thyroid nodules do not need treatment unless they induce local compressive symptoms which include dysphagia, swallowing, shortage of breath, a raspy voice or anxiety. In these circumstances, a thyroidectomy is recommended. [52].

A single poisonous nodule or a toxic multinodular goiter are two other benign nodule indications that may necessitate surgery. Radioiodine (131I) therapy is another option for treating toxic nodular goiters; however, because these goiters are often more radio resistant than toxic diffuse goiters, it is not the first line of treatment if compressive symptoms are present. Larger nodules are likewise not suggested for 131-I treatment since they require higher doses and are associated with unfavorable side effects. When treating patients with uncontrolled thyrotoxicosis, radioiodine therapy must be used carefully. Pregnancy and lactation, however, are the only absolute contraindications to 131-I treatment. [53].

The preferred treatment for thyroid cysts is aspiration; nevertheless, recurrence rates are substantial (60–90% of patients), especially in cases of large-volume cysts and recurrent aspirations [54]. Numerous sizable randomized controlled trials have examined percutaneous ethanol injection (PEI), and after an average of two sessions, 82–85% of the patients were found to be successful, this results in a volume decrease of more than 85% from the baseline size. PEI is another possibility for high-functioning nodules, particularly if there is a considerable fluid component. It has a mean volume decrease of 66% and a success rate ranging from 64% to 95%; however, recurrences are more common, and more sessions are required to obtain a successful response (approximately 4 sessions per patient) [55]. PEI is a safe surgery; the most common adverse effects recorded are flushing, disorientation, local pain, dysphonia, and, in rare cases, recurrence laryngeal damage. In addition to being a realistic treatment for toxic mononuclear goiter and solitary toxic nodules, surgery is a reasonable treatment for cystic lesions in place of the aforementioned procedures. Levothyroxine (T4) therapy for benign thyroid nodules has been proposed as a method of reducing nodule size and preventing new nodules from developing by decreasing TSH levels. While a number of randomized control trials and meta-analyses have shown that patients from iodine-deficient areas experience nodule reduction, only a small percentage of patients with adequate iodine intake experience a clinically significant drop in nodule volume. Colloid appearance during FNA, small nodule size, and recent diagnosis are further prognostic factors of good response to T4 treatment. [56].

Adverse consequences of T4 suppressive medication include atrial fibrillation, decreased bone density, particularly in postmenopausal women, and increased overall morbidity and mortality from cardiovascular disease. According to current guidelines, patients with benign thyroid nodules from iodine-rich areas should not be given T4 suppression medication on a regular basis. A recent inquiry for harmless goiters was conducted in Italy. However, as compared to an untreated population, a recent Italian study on patients with non-toxic goiters found reduced goiter development, decreased formation of new nodules, and a lower risk of developing PTC in the T4-receiving population [57]. As a result, this management strategy could be useful.

FURTHER INVESTIGATION:

A 50% increase in the volume of a previously biopsied thyroid nodule is a valid reason to repeat a FNA. Because there is a 5% probability of false-negative results after the initial FNA, Benign thyroid nodules demand extended follow-up [58]. Serial US is the recommended study for thyroid nodule follow-up, and it should be performed 6 to 18 months after the initial FNA to detect significant changes in size or appearance.

THYROID NODULES IN PREGNANCY:

In case thyroid cancer is detected during pregnancy, it is typically recommended to postpone surgery until after the baby is born.

For thyroid cancer that is aggressive or growing quickly, the safest time for surgery is during the second trimester of pregnancy.

It is uncertain what causes thyroid nodules found during pregnancy and how they behave in relation to the general population [61]. Therefore, with the exception of the patient's contraindication to radionuclide scanning, the examination ought to be comparable to that of non-pregnant patients. The radionuclide scan and any necessary FNA after the first trimester can be safely delayed until after delivery and the end of lactation if a patient is discovered to have continuously suppressed blood TSH levels [17]. Consensus guidelines advise doing a FNA biopsy on pregnant women with thyroid nodules who are euthyroid or hypothyroid. [17]. However, there is a case to be made for postponing the FNA until after delivery, barring concerning clinical characteristics that could suggest a thyroidectomy during pregnancy. If the FNA resulted in a malignancy diagnosis, but the planned strategy before to the FNA was to postpone the thyroidectomy until the patient was postpartum, this will only cause the patient to become anxious about a diagnosis over which she has no control.

Previous studies have indicated that expecting patients diagnosed with PTC behave similarly to the general population, with no changes in survival rates or recurrences in pregnant women operated on for PTC during or after birth. [62].

However, pregnant women have a larger risk of problems following thyroid surgery than non-pregnant women. Postponing surgery until after birth looks to be a viable option, as recent retrospective data indicate that waiting less than a year following a differentiated thyroid cancer diagnosis has no impact on the patient's health. Surgery should be performed in the second trimester of pregnancy if the illness is more progressed or aggressive at the time of diagnosis, or if thyroidectomy is chosen for thyroid cancer detected early in pregnancy to lower the risk of miscarriage and premature birth. [63].It is recommended to take T4 suppressive medication to keep serum TSH levels between 0.1 and 1.0 mU/L in pregnant women who have been diagnosed with thyroid cancer via FNA and are undergoing thyroidectomy [64].

DIFFERENTIAL DIAGNOSIS:

Although the majority of Nodules and masses in the anterior neck are benign thyroid nodules or cysts; malignancy should be ruled out, particularly in patients who are at risk for thyroid cancer. [65]. Congenital neck masses can occur in the anterior neck. The majority of these are present at birth, while others may appear in adulthood. The higher the age at presentation, the greater the risk of malignancy. Tongue, tonsil, and thyroid malignancies can all generate cystic neck tumors. Inflammatory neck masses are most commonly caused by enlarged lymph nodes, which can be bacterial or viral in origin. These are usually located anterior to the trapezius muscle and superficial, deep, or posterior to the sternocleidomastoid muscle [65].

Metastatic neck masses are a common symptom of non-thyroid neoplastic illnesses. These are commonly associated with squamous cell carcinoma of the gastrointestinal tract. [66].

PROGNOSIS:

Thyroid nodules are typically benign. Initial observations, such as MEN or radiation history, normal to high serum TSH levels, and certain ultra-sonographic features, raise suspicions of cancer. Although the risk of cancer is higher in single nodules than in nodules within a multinodular thyroid, the total risk of cancer is comparable due to the cumulative danger of each nodule in a multinodular gland. [67].

The prognosis of thyroid cancer is highly influenced by its histological type and subtype, as well as a number of individual factors such as the patient's age at diagnosis, the size of the primary tumor, the presence of soft tissue invasion, and distant metastases [67]. The majority of patients with papillary thyroid carcinoma do not die from the disease. A case series of persons with papillary thyroid carcinoma who were not metastatic revealed a 6% malignancy-related death rate. [68].Male gender, mediastinal lymph node involvement, delay in main surgical therapy of more than 1 year following nodule discovery, and multicentricity of the intrathyroidal carcinoma are all associated with an elevated risk of malignancy recurrence or fatality.[68]. Follicular cancer patients tend to be older and have a history of aggressive disease. It is typically associated with a higher death rate and distant metastases than papillary thyroid cancer [69].

COMPLICATIONS:

Patients with functioning thyroid nodules may experience complications, including hyperthyroidism symptoms. Clinical signs and symptoms will include symptoms associated with hyperthyroidism, including palpitations, sweating, and decreased glucose tolerance. On the other hand, most thyroid nodules are benign, and the majority of patients experience no symptoms [70].

Thyroid pain is a rare symptom that some individuals experience; it is more common in those with cystic thyroid lesions and may be an indication of hemorrhagic infarction or abrupt bleeding. [70].

SONO-ELASTOGRAPHY:

A sono-elastography, another name for ultrasound elastography, is a contemporary, evolving technique for sonographic imaging. Among the methods are strain elastography, often referred Static or compression elastography, and shear wave elastography, also known as transient elastography. These methods use sound

waves to analyze the mechanical properties of tissues. For example, their elasticity and stiffness in reaction to mechanical pressure. Through the utilization of the variations in the previously mentioned mechanical properties, they are employed to identify various diseases in tissues. [71].
Because of its predictive relevance Ultrasound elastography is increasingly employed as a non-invasive method for grading and determining the amount of liver fibrosis in chronic liver disease. [71].

PHYSICS
The measurement of tissue stiffness is based on a physical property known as Young's modulus, or modulus of elasticity. Young's modulus is calculated by dividing the stress. (The force applied to a specific area) of a particular material by its strain (in this case, the tissue's deformation) [72].

APPLICATIONS
Sonographic elastography has numerous clinical uses and is used to assess the degree of hepatic fibrosis and characterize the liver.
Lesions to assess diffuse renal parenchymal changes and
Characterization of renal lesions [72]

- in breast mis- diagnosis
- in prostate cancer detection
- in thyroid lesion characterization
- in tendon imaging

OBJECTIVE
In patients who have a suspicious lesion on thyroid ultrasonography at a tertiary care hospital in Karachi, the objective is to ascertain the diagnostic accuracy of sonoelastography in the diagnosis of malignant thyroid nodules, with histology serving as the gold standard.

OPERATIONAL DEFINITION:
SUSPICIOUS THYROID NODULE
Patients underwent thyroid ultrasound were labeled as suspicious nodule for malignancy by the presence of any one or more of the Following:

- Echogenicity: Hypo-echoic thyroid nodule relative to the adjacent normal thyroid tissue.
- Size: Thyroid nodule size ≥ 1 cm with anteroposterior (AP) diameter of thyroid nodule was more than transverse (TR) diameters.
- Margins: Irregular margins of thyroid nodule (loss of halo sign).
- Calcifications: Hyper-echoic foci of calcifications within thyroid nodule.
- Vascularity: Grade II intranodular vascularity (ANNEXURE A).

MALIGNANT THYROID NODULE ON SONOELASTOGRAPHY
Patients underwent sonoelastography and were assessed on the basis of Rago Criteria (Qualitative evaluation system for thyroid nodules on a scale of 1 to 5). Nodules with Rago scores more than 4 were classified as malignant.

MALIGNANT THYROID NODULE ON HISTOPATHOLOGY
A nodule was classified as malignant if its histology revealed any of the following: (ANNEXUREB)

- Papillary cancer.
- Follicular carcinoma.
- Hurthle cell (oncocytic) carcinoma.
- Medullary cancer.
- Anaplastic cancer.

TRUE POSITIVE
Patients with malignancy on histopathology and sonoelastography had a Rago scores of≥ 4.
TRUE NEGATIVE
Patients without malignancy sonoelastography had a Rago scores of ≤ 4.

FALSE POSITIVE
Patients without malignancy on histopathology and malignant on sonoelastography had a Rago scores of≥ 4.
FALSE NEGATIVE
Patients with malignancy on histopathology and no malignancy on sonoelastography had a Rago scores of ≤ 4.

DIAGNOSTIC ACCURACY
Total Positive + Total Negative/total patients x 100
SENSITIVITY
The percentage of positives that were accurately classified as having the disease was determined by sensitivity. True Negative/False Negative plus True Positive**.**

SPECIFICITY
The percentage of negatives that were accurately classified as not having the ailment was measured as specificity. True Negative/False Positive + True Negative.

POSITIVE PREDICTIVE VALUE
The percentages of real positive results in diagnostic tests and statistics were known as positive predictive values. True + False Positive or True plus Positive.

NEGATIVE PREDICTIVE VALUE
Negative predictive values are the proportion of false negative results in statistics and diagnostic testing. Positive Negative + Negative False or Both.
DIAGNOSTIC PRECISION
Total Positive + Total Negative/total patients x 100

Research of Medical Science Review

MATERIAL & METHODS
STUDY DESIGN
Cross-Sectional Study.

STUDY SETTING
Department of Radiology, Sindh Institute of Urology & Transplantation (SIUT)), Karachi.
DURATION OF STUDY
Six months after the approval of synopsis from July 23, 2020 to January 22, 2021.

SAMPLE SIZE
The sample size was determined by taking into account the following factors: 42% of malignant nodules, sensitivity of 86%[14], specificity of 66.7%[14], margin of error of 10% for sensitivity, d=8% for specificity, and confidence interval of 95%. As a result, 174 patients were considered to be the sample size.
SAMPLING TECHNIQUE
Non-Probability, Consecutive Sampling.

SAMPLE SELECTION

INCLUSION CRITERIA:

- According to the operational criteria, patients who had a worrisome thyroid nodule for longer than a month were included.
- Either gender.
- 20 to 60 years of age.

EXCLUSION CRITERIA:

- Not giving consent.
- Individuals who have previously experienced diffuse or multinodular goiter.
- Patients with history of hypothyroidism or hyperthyroidism.
- Individuals who have a past history of cancer.
- Patient with uncontrolled hypertension (BP> 160 mmHg systolic and >90 mmHg diastolic.
- Individuals who have a history of type II diabetes.
- Expectant individuals evaluated based on their medical history and verified with a dating scan.

Individuals having a history of stroke, renal impairment, asthma, CCF, or chronic obstructive pulmonary disease were not accepted.

DATA COLLECTION

This study was conducted with approval from the College of Physicians and Surgeons Pakistan. The Department of Radiology, SIUT, Karachi, enrolled study participants who were considered patients and who fulfilled the inclusion criteria in the operational definition. The institutional ethical review committee's approval was obtained before the study could begin. Prior to being assigned to a sample or having their data utilized in research, every patient provided their informed consent. Brief historical information was gathered in order to action about the patient's gender, place of residence, and length of symptoms (mass and neck discomfort). Under the operational definition, all patients with a suspicious nodule on thyroid ultrasound had sonoelastography, which was carried out in the researcher's presence by the same radiologist with more than 10 years of expertise. Utilizing the Using split-screen technology, the elastography feature was activated for the sonoelastography method using the same probe. On the right side of the screen, the US elastogram image was superimposed over the B mode image. Green represented intermediate elasticity on the color scale, which went from red for the components with the maximum elastic strain (softest) to blue for the components with no strain (hardest). Images were displayed on the left side of the screen using B-mode sonography to compare the two perspectives of the same scan plane. Nodules with Rago values greater than 4 on sonoelastography were considered malignant. Following the operational criteria, the researcher monitored the patients and documented the postoperative histology report for malignancy. Age and length of symptoms were the quantitative variables, and gender, residence status, family monthly income, employment status, thyroid nodule malignancy verified by sonoelastography (Positive/Negative), and histopathology (Positive/Negative) were the qualitative variables. The results were entered into an annexured Performa.

DATA ANALYSIS

With SPSS Version 20, the data analysis was carried out. For continuous factors like age and duration of symptoms, the mean and standard deviation were computed. Frequency and percentage estimates were made for the following factors: gender, residency status, family monthly income, job status, thyroid nodule malignancy confirmed by sonoelastography (Positive/Negative), and histology (Positive/Negative). The diagnostic precision, sensitivity, specificity, positive and negative predictive values, and specificity of the sonoelastography were calculated utilizing using histology as the benchmark. Age, gender, domicile status, monthly household income, work status, and length of symptoms were all stratified. Post-calculations were performed to determine the diagnostic accuracy, specificity, sensitivity, negative and positive predictive values, and stratification.

RESULTS

In this study, 174 patients from a tertiary care hospital in Karachi who had suspicious thyroid ultrasonography nodules were recruited to evaluate the diagnostic accuracy of sonoelastography in detecting malignant thyroid nodules, with histology being the gold standard. The outcomes were examined as follows:

Mean ± SD of age was 37.7±7.2 with C.I (36.62…….38.77) years as shown in TABLE1.

Mean ± SD of duration of symptoms was 6.5±2.4 with C.I (6.14…….6.85) months as shown in TABLE2.

In distribution of gender, 64 (36.8%) patients were male while 110 (63.2%) were female patients as shown in

FIGURE 7.

Out of 174 patients, 123 (70.7%) Patients lived in cities, whereas 51 people (29.3%) lived in rural areas, as demonstrated in

FIGURE 8.

Out of 174 patients, 78 (44.8%) patients were employed while 96 (55.2%) were unemployed as shown in

FIGURE 9

In distribution of family monthly income 19 (11%) were belong to lower income group, 65 (37.3%) were lower middle-income group, 42

(24.1%) middle-income group, 28(16.1%) upper-middle-income group while 20 (11.5%) patients were belonged to upper income group as shown in

TABLE 3.

On sonoelastography malignant thyroid nodule was noted in 97 (55.7%) patients as shown in FIGURE 10.

Malignant thyroid nodule was diagnosed in 46 (26.4%) patients on histopathology (gold standard) as shown in

FIGURE 11.

Using histopathology as the gold standard, the diagnostic accuracy of sonoelastography was shown to be 70.69% in the identification of a malignant thyroid nodule, with sensitivity of 84.78%, specificity of 57.40%, PPV of 46.99%, and NPV of 92.31%.

TABLE4.

Stratification of age group, gender, duration of symptoms, residential status and occupational status were done with respect to

Sonoelastography to find statistical difference from TABLE [5—9].

DISCUSSION

Thyroid nodules were frequently observed since they were discovered in 4–8% of adult cases by palpation, 10–41% by purposeful or accidental ultrasound, and 50% by pathologic investigation at postmortem [73]. Despite the high incidence of nodules, thyroid cancer is rather uncommon, with fewer than 6% of all nodules becoming malignant. Fortunately, early detection and treatment can greatly improve the prognosis of thyroid tumors [74].

Typical cancer presentation since thyroid is a solid solitary nodule, it is critical to distinguish between benign and malignant causes. Consequently, developing a system to identify nodule candidates for fine needle aspiration cytology is necessary. [74, 75].

Beyond verifying the existence of thyroid nodules and evaluating their size, texture, and vascularity, ultrasound is highly useful since it provides valuable information regarding the qualitative classification of thyroid nodules according to benign or malignant characteristics. [76, 77].

Given that more firm nodules are more likely to be malignant, skilled hand palpation can provide an early indication of a nodule's stiffness and, consequently, raise the probability that the nodule is malignant. Conversely, deep or tiny nodules are rarely assessed by palpation; instead, sono-elastography (USE), a form

of elasticity imaging, has been employed recently. USE uses customized software in conjunction with complementary standard US systems to estimate the mechanical characteristics of tissue in vivo. [78, 79].

The concept behind its use is based on low-amplitude, low-frequency shear waves that go through the thyroid gland. Wherever there is a hard inhomogeneity—such as a tumor—the vibration amplitude at that area will drop. Stiff tissue exhibits less strain than softer tissue when a specific applied force is applied. Thus, we can determine tissue stiffness by measuring the strain on tissue caused by compression. [80, 81].

Because of its superficial and anterior location, the thyroid gland is in a good position for electrographic testing and can be readily crushed against According to basic principles of sonoelastography, the elastic modulus of malignant thyroid nodules is predicted to be substantially higher than that of benign and normal thyroid tissue, establishing the concept for the application of USE in nodule nature assessment. [84-86].

Depending on color changes or a numerical estimate of the degree of stiffness, many variable sonoelastography scores are applied.

The most often used grading system is Rago's, which uses a color-coded scale of 1 to 5 to assess thyroid nodules qualitatively. Green indicates a benign nodule, while the color blue denotes a malignant one. [87].

In addition to the color scale, other numerical techniques such determining the strain ratio—which is defined as the ratio of stiffness between the nodular tissue and the surrounding normal thyroid tissue—may be useful in distinguishing benign from malignant solitary thyroid nodules. [88].

The Bethesda Thyroid Atlas Project was created based on the NCI meeting's results regarding terminology and morphologic criteria, which also serve as the foundation for The Thyroid Cytopathology Reporting System from Bethesda (TBSRTC). The Bethesda classification is divided into six groups based on the level of cancer risk associated with suggested clinical care [89].

Sonoelastography (USE) improved the diagnostic performance of grayscale US as the gland was suitable technically for effective compression against underlying anatomic tissues with a US probe, allowing for a sufficient assessment of the thyroid nodules' elastic nature [90, 91].

Thyroid nodules are widespread, particularly in regions with low iodine levels. Actually, palpable nodules can be seen in as much as 5% of the general population, and thyroid nodules can be found in as much as 50% of the general population at autopsy or sonography [87, 91]. Thyroid nodules, however, hardly ever develop into cancer [87]. The primary diagnostic technique for thyroid nodules is cytologic analysis of a sample taken during invasive FNA, despite the fact that this is typically a difficult medical diagnosis. In addition to being intrusive, FNA has drawbacks. Up to 30% of FNA samples from thyroid nodules produce cytologic results that are inconclusive; 15% of FNA samples yield nondiagnostic results, and 10%–20% yield uncertain results. The insufficient cell sample is the cause of these diagnostic failures. Hemorrhagic cysts, multinodular goiter, or nodules ranging in size from 1 to 4 cm [91]. As opposed to its sensitivity, FNA cytology actually has a high specificity [87]. Differentiating between benign and malignant cells can be challenging or impossible in certain FNA samples that include sufficient cells. This is particularly true when attempting to distinguish between benign follicular adenoma and follicular carcinoma or follicular papillary cancer [87]. A cytologist's experience may determine whether or not to detect up to 30% of cancerous thyroid nodules. Particularly if the patient has a fibrotic thyroid or multinodular goiter, or if the nodules are tiny or dorsally situated. [86, 87].

In our study, mean age was 37.7±7.2 years. Afifi AH, et al [16] reported age as 38 years.

110 (63.2%) of the study's patients were female, and 64 (36.8%) were male. Twenty males (40%) and thirty females (60%) were enrolled in the Afifi AH, et al. research project. [16].

In the current investigation, 97 (55.7%) individuals had a malignant thyroid nodule detected on sonoelastography. Malignant thyroid nodule was reported by Ghajarzadeh M, et al. [14] to be 363 (30.76%). 46 patients (26.4%) had a malignant thyroid nodule identified by histology (gold standard). The results of Afifi AH, et al. included 21 (42%) pathologically proven malignant nodules for documentation. [16].

Using histology as the gold standard, the current study found that sonoelastography had a 70.69% diagnostic accuracy in the identification of a malignant thyroid nodule, with a sensitivity of 84.78%, specificity of 57.40%, PPV of 46.99%, and NPV of 92.31%. Ghajarzadeh M. et al.'s study [14] revealed sensitivity of 86%

and specificity of 66.7%, while Afifi AH. et al. similarly reported sensitivity of 92%, specificity of 95%, and PPV of 89%. NPV 92% and precision of diagnosis 96% [16].

CONCLUSION

It can be inferred that every instance of a malignant thyroid nodule should be investigated by histopathology. Since using histology to evaluate thyroid nodules did not appear to be beneficial or equivalent to sonoelastography. Throughout order to validate the results of this study, other large-scale local investigations including numerous study centers throughout Pakistan must be conducted in the future.

REFERENCES

Xing P, Wu L, Zhang C, Li S, Liu C, Wu C. Differentiation of benign from malignant thyroid lesions: calculation of the strain ratio on thyroid sonoelastography. J Ultrasound Med 2011;30:663–9.

Cappelli C, Castellano M, Pirola I. Thyroid nodule shape suggests malignancy. Eur J Endocrinol 2006;155:27–31.

Asteria C, Giovanardi A, Pizzocaro A. US elastography in the differential diagnosisof benign and malignant thyroid nodules. Thyroid 2008;18:523–31.

Garra BS. Elastography: current status, future prospects, and making it work foryou. Ultrasound Q 2011;27:177–86.

Bhatia KSS, Rasalkar DP, Lee YP. Cystic change in thyroid nodules: a confounding factor for real-time qualitative thyroid ultrasound elastography. Clin Radiol 2011;66:799-07.

Cakir B, Aydin C, Korukluoğlu B, Ozdemir D, Sisman IC, Tüzün D, et al. Diagnostic value of elastosonographically determined strain index in the differential diagnosis of benign and malignant thyroid nodules. Endocrine. 2011;39(1):89-98.

Friedrich-Rust M, Sperber A, Holzer K Diener J, Grünwald F, Badenhoop K, et al. Real- time elastography and contrast-enhanced ultrasound for the assessment ofthyroid nodules. Exp Clin Endocrinol Diabetes 2010;118:602–9.

Gietka-Czernei M, Kochman M, Bujalska K, Stachlewska-Nasfeter E, Zgliczyński W. Realtime ultrasound elastography: a new tool for diagnosing thyroid nodules. Endokrynol Pol 2010;61:652–57.

Kagoya R, Monobe H, Tojima H. Utility of elastography for differential diagnosis of benign and malignant thyroid nodules. Otolaryngol Head Neck Surg2010;143:230–34.

Rubaltelli L, Corradin S, Dorigo A, Stabilito M, Tregnaghi A, Borsato S, et al. Differential diagnosis of benign and malignant thyroid nodules at elastosonography. Ultraschall Med 2009;30:175–9.

Wang Y, Dan HJ, Dan HY, Li T, Hu B. Differential diagnosis of small single solid thyroid nodules using real-time ultrasound elastography. J Int Med Res 2010;38:466–72.

Trimboli P, Guglielmi R, Monti S. Ultrasound sensitivity for thyroid malignancy isincreased by real-time elastography: a prospective multicenter study. J Clin Endocrinol Metab 2012;97(12):4524–30.

Huang R, Jiang L, Xu Y, Gong Y, Ran H, Wang Z, et al. Comparative diagnostic accuracy of contrast-enhanced ultrasound and shear wave elastography in differentiating benign and malignant lesions: a network meta-analysis. FrontOncol. 2019;9:102.

Ghajarzadeh M, Sodagari F, Shakiba M. Diagnostic accuracy of sonoelastography in detecting malignant thyroid nodules: a systematic review and meta-analysis. Am J Radiol 2014;202:W379–89.

Tian W, Hao S, Gao B, Jiang Y, Zhang S, Guo L, Luo D. Comparison of diagnostic accuracy of real-time elastography and shear wave elastography in differentiation malignant from benign thyroid nodules. Medicine (Baltimore). 2015;94(52):e2312.

Afifi AH, Alwafa WAH, Aly WM, Alhammadi HAB. Diagnostic accuracy of thecombined use of conventional sonography and sonoelastography in differentiating benign and malignant solitary thyroid nodules. Alex J Med 2017:53:21–30.

Cooper DS. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009;19(11):1167–214.

Marqusee E, Benson CB, Frates MC, Doubilet PM, Larsen PR, Cibas ES, et al. Usefulness of ultrasonography in the management of nodular thyroid disease. Ann Intern Med. 2000;133(9):696-700.

Mortensen JD, Woolner LB, Bennett WA. Gross and microscopic findings in clinically normal thyroid glands. J Clin Endocrinol Metab. 1955;15(10):1270–80.

Tan GH, Gharib H. Thyroid incidentalomas: management approaches to non-palpable nodules discovered incidentally on thyroid imaging. Ann Intern Med. 1997;126(3):226– 31.

Antonelli A, Silvano G, Bianchi F, Gambuzza C, Tana L, Salvioni G, et al. Risk of thyroid nodules in subjects occupationally exposed to radiation: a cross sectional study. Occup Environ Med. 1995;52(8):500-4.

Kovács GL, Gonda G, Vadász G, Ludmány É, Uhrin K, Görömbey Z, et al. Epidemiology of thyroid microcarcinoma found in autopsy series conducted in areas of different iodine intake. Thyroid. 2005;15(2):152-7.

Kang KW, Kim SK, Kang HS, Lee ES, Sim JS, Lee IG, et al. Prevalence and risk of cancer of focal thyroid incidentaloma identified by 18F-fluorodeoxyglucose positron emission tomography for metastasis evaluation and cancer screening in healthy subjects. J Clin Endocrinol Metab. 2003;88(9):4100-4.

Hemminki K, Eng C, Chen B. Familial risks for nonmedullary thyroid cancer. J Clin Endocrinol Metab. 2005;90(10):5747–53.

Lloyd KM, 2nd, Dennis M. Cowden's disease. A possible new symptom complex with multiple system involvement. Ann Intern Med. 1963;58:136–42.

Liaw D, Marsh DJ, Li J, Dahia PL, Wang SI, Zheng Z, et al. Germline mutations of the PTEN gene in Cowden disease, an inherited breast and thyroid cancer syndrome. Nat Genet. 1997;16(1):64-7.

Saad AG, Kumar S, Ron E, Lubin JH, Stanek J, Bove KE, Nikiforov YE. Proliferative activity of human thyroid cells in various age groups and its correlation with the risk of thyroid cancer after radiation exposure. J Clin Endocrinol Metab. 2006;91(7):2672-7.

Walfish PG, Strawbridge HT, Rosen IB. Management implications from routine needle biopsy of hyperfunctioning thyroid nodules. Surgery. 1985;98(6):1179-88.

Welker MJ, Orlov D. Thyroid nodules. Am Fam Physician. 2003;67(3):559-66.

Bomeli SR, LeBeau SO, Ferris RL. Evaluation of a thyroid nodule. Otolaryngol Clin North Am. 2010;43(2):229-38.

Yeung MJ, Serpell JW. Management of the solitary thyroid nodule. Oncologist. 2008;13 (2):105-12.

Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedüs L, et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations. J Endocrinol Invest. 2010;33(Suppl 5):51–6.

Jimenez C, Hu MI, Gagel RF. Management of medullary thyroid carcinoma. Endocrinol Metab Clin North Am. 2008;37(2):481–96.

Cheung K, Roman SA, Wang TS, Walker HD, Sosa JA. Calcitonin measurement in the evaluation of thyroid nodules in the United States: a cost-effectiveness and decision analysis. J Clin Endocrinol Metab. 2008;93(6):2173–80.

Gharib H, Papini E. Thyroid nodules: clinical importance, assessment, and treatment. Endocrinol Metab Clin North Am. 2007;36(3):707–35.

Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and colordoppler features. J Clin Endocrinol Metab. 2002;87(5):1941-6.

Papini E. The dilemma of non-palpable thyroid nodules. J Endocrinol Invest. 2003;26(1): 3–4.

Moon WJ, Jung SL, Lee JH, Na DG, Baek JH, Lee YH, et al. Benign and malignant thyroid nodules: US differentiation—multicenter retrospective study. Radiology. 2008;247(3): 762-70.

Bojunga J, Herrmann E, Meyer G, Weber S, Zeuzem S, Friedrich-Rust M. Real-time elastography for the differentiation of benign and malignant thyroid nodules: a metaanalysis. Thyroid. 2010;20(10):1145-50.

Danese D, Sciacchitano S, Farsetti A, Andreoli M, Pontecorvi A. Diagnostic accuracy of conventional versus sonography-guided fine-needle aspiration biopsy of thyroid nodules. Thyroid. 1998;8(1):15-21.

Fraker DL. Thyroid tumors. In: HS De Vita V Jr, Rosenberg S, editors. Cancer: principles and practice of oncology. Lippincott-Raven; Philadelphia: 1997. pp. 1629–52.

Yeh MW, Demircan O, Ituarte P, Clark OH. False-negative fine-needle aspiration cytology results delay treatment and adversely affect outcome in patients with thyroid carcinoma. Thyroid. 2004;14(3):207-15.

Baloch ZW, LiVolsi VA, Asa SL, Rosai J, Merino MJ, Randolph G, et al. Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: a synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. Diagn Cytopathol. 2008;36(6):425-37.

Gharib H, Goellner JR. Fine-needle aspiration biopsy of thyroid nodules. Endocr Pract. 1995;1(6):410–7.

Meko JB, Norton JA. Large cystic/solid thyroid nodules: a potential false-negative fineneedle aspiration. Surgery. 1995;118(6):996–1003.

Baloch ZW, Fleisher S, LiVolsi VA, Gupta PK. Diagnosis of "follicular neoplasm": a gray zone in thyroid fine-needle aspiration cytology. Diagn Cytopathol. 2002;26(1):41-4.

Nikiforov YE, Ohori NP, Hodak SP, Carty SE, LeBeau SO, Ferris RL, et al. Impact of mutational testing on the diagnosis and management of patients with cytologically indeterminate thyroid nodules: a prospective analysis of 1056 FNA samples. J Clin Endocrinol Metab. 2011;96(11):3390-7.

Li H, Robinson KA, Anton B, Saldanha IJ, Ladenson PW. Cost-effectiveness of a novel molecular test for cytologically indeterminate thyroid nodules. J Clin Endocrinol Metab. 2011;96(11):E1719-26.

Chudova D, Wilde JI, Wang ET, Wang H, Rabbee N, Egidio CM, et al. Molecular classification of thyroid nodules using high-dimensionality genomic data. J Clin Endocrinol Metab. 2010;95(12):5296-304.

Milas M, Shin J, Gupta M, Novosel T, Nasr C, Brainard J, et al. Circulating thyrotropin receptor mRNA as a novel marker of thyroid cancer: clinical applications learned from 1758 samples. Ann Surg. 2010;252(4):643-51.

Giovanella L, Suriano S, Maffioli M, Ceriani L. 18FDG-positron emission tomography/ computed tomography (PET/CT) scanning in thyroid nodules with nondiagnostic cytology. Clin Endocrinol. 2011;74(5):644-8.

Frates MC, Benson CB, Doubilet PM, Kunreuther E, Contreras M, Cibas ES, et al. Prevalence and distribution of carcinoma in patients with solitary and multiple thyroid nodules on sonography. J Clin Endocrinol Metab. 2006;91(9):3411-7.

Lazarus JH. Guidelines for the use of radioiodine in the management of hyperthyroidism: a summary. Prepared by the Radioiodine Audit Subcommittee of the Royal College of Physicians Committee on Diabetes and Endocrinology, and the Research Unit of the Royal College of Physicians. J R Coll Physicians Lond. 1995;29(6):464–9.

Bennedbaek FN, Hegedus L. Treatment of recurrent thyroid cysts with ethanol: a randomized double-blind controlled trial. J Clin Endocrinol Metab. 2003;88(12):5773–7.

Tarantino L, Francica G, Sordelli I, Sperlongano P, Parmeggiani D, Ripa C, et al. Percutaneous ethanol injection of hyperfunctioning thyroid nodules: long-term followup in 125 patients. Am J Roentgenol. 2008; 190(3):800-8.

Verde G, Papini E, Pacella CM. Ultrasound guided percutaneous ethanol injection in the treatment of cystic thyroid nodules. Clin Endocrinol (Oxf) 1994;41(6):719–24.

La Rosa GL, Ippolito AM, Lupo LO, Cercabene GI, Santonocito MG, Vigneri RI, et al. Cold thyroid nodule reduction with L-thyroxine can be predicted by initial nodule volume and cytological characteristics. J Clin Endocrinol Metab. 1996;81(12):4385-7.

Carmeci C, Jeffrey RB, McDougall IR, Nowels KW, Weigel RJ. Ultrasound-guided fineneedle aspiration biopsy of thyroid masses. Thyroid. 1998;8(4):283-9.
Brauer VF, Eder P, Miehle K, Wiesner TD, Hasenclever H, Paschke R. Interobserver variation for ultrasound determination of thyroid nodule volumes. Thyroid. 2005;15(10): 1169-75.
Oertel YC, Miyahara-Felipe L, Mendoza MG, Yu K. Value of repeated fine needle aspirations of the thyroid: an analysis of over ten thousand FNAs. Thyroid. 2007;17(11): 1061-6.
Tan GH, Gharib H, Goellner JR, Van Heerden JA, Bahn RS. Management of thyroid nodules in pregnancy. Arch Intern Med. 1996;156(20):2317-20.
Moosa M, Mazzaferri EL. Outcome of differentiated thyroid cancer diagnosed in pregnant women. J Clin Endocrinol Metab. 1997;82(9):2862–6.
Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. Am J Med. 1994;97(5):418–28.
Rosen IB, Korman M, Walfish PG. Thyroid nodular disease in pregnancy: current diagnosis and management. Clin Obstet Gynecol. 1997;40(1):81–9.
Alvi A, Johnson JT. The neck mass. A challenging differential diagnosis. Postgrad Med. 1995;97(5):87-90.
Lin ST, Tseng FY, Hsu CJ, Yeh TH, Chen YS. Thyroglossal duct cyst: a comparison between children and adults. Am J Otolaryngol. 2008;29(2):83-7.
Gluckman JL, Robbins KT, Fried MP. Cervical metastatic squamous carcinoma of unknown or occult primary source. Head Neck. 1990;12(5):440-3.
Tuttle RM. Risk-adapted management of thyroid cancer. EndocrPract. 2008;14(6):76474.
Grebe SK, Hay ID. Follicular thyroid cancer. Endocrinol Metab Clin North Am. 1995;24(4): 761-801.
Tan GH, Gharib H. Thyroid incidentalomas: management approaches to nonpalpable nodules discovered incidentally on thyroid imaging. Ann Intern Med. 1997;126(3):226-31.
Smajlović F, Čarovac A, Bulja D. Sonoelastography: the method of choice for evaluation of tissue elasticity. J Health Sci. 2011;1(1):50-5.
Pan X, Huang J, Feng N, Chen S. A novel young's modulus reconstruction method based on a modified plane-strain model. J Med Imaging Health Inform. 2018;8(5):915-24.
Alexander EK, Marqusee E, Orcutt J, Benson CB, Frates MC, Doubilet PM, et al. Thyroid nodule shape and prediction of malignancy. Thyroid. 2004;14(11):953-8.
Papini E, Guglielmi R, Bianchini A, Crescenzi A, Taccogna S, Nardi F, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and colorDoppler features. J Clin Endocrinol Metab. 2002;87(5):1941-6.
Hegedu¨s L. Clinical practice. The thyroid nodule. N Engl J Med 2004;351(17):1764–71.
Lew JI, Solorzano CC. Use of ultrasound in the management of thyroid cancer. Oncologist 2010;24:2009–32.
Ozel A, Erturk SM, Ercan A, Yılmaz B, Basak T, Cantisani V, et al. The diagnostic efficiency of ultrasound in characterization for thyroid nodules: how many criteria are required to predict malignancy? MedUltras. 2012;14(1):24-8.
Garra BS, Cespedes EI, Ophir J. Elastography of breast lesions: initial clinical results. Radiology 1997;202:79–86.
Lyshchik A, Higashi T, Asato R. Thyroid gland tumor diagnosis at US elastography. Radiology 2005;237:202–11.
Tranquart F, Bleuzen A, Pierre-Renoult P, Chabrolle C, Lecomte P. Elastosonography of thyroid lesions. J Radiol2008;89:35–9.
Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, et al. Breast disease: clinical application of US elastography for diagnosis(1). Radiology 2006;239(2):341–50.
Park SH, Kim SJ, Kim EK, Kim MJ, Son EJ, Kwak JY. Interobserver agreement in assessing the sonographic and elastographic features of malignant thyroid nodules. Am J Roentgenol. 2009;193(5):W416-23.
Lyshchik A, Higashi T, Asato R, Tanaka S, Ito J, Mai JJ, et al. Thyroid gland tumor diagnosis at US elastography. Radiology 2005;237(1):202–11.

Lim DJ, Luo S, Kim MH, Ko SH, Kim Y. Interobserver agreement and intraobserver reproducibility in thyroid ultrasound elastography. Am JRoentgenol 2012;198(4):896– 901.

Ciledag N, Arda K, Arıbas BK, Aktas E, Köse SK. The utility of ultrasound elastography and MicroPure imaging in the differentiation of benign and malignant thyroid nodules. Am J Roentgenol 2012;198(3):W244–9.

Bojunga J, Herrmann E, Meyer G, Weber S, Zeuzem S, Friedrich-Rust M. Real-time elastography for the differentiation of benign and malignant thyroid nodules: a metaanalysis. Thyroid 2010;20(10):1145–50.

Rago T, Santini F, Scutari M, Pinchera A, Vitti P. Elastography: new developments in ultrasound for predicting malignancy in thyroid nodules. J Clin Endocrinol Metab 2007;92(8):2917-22.

Ning CP, Jiang SQ, Zhang T, Sun LT, Liu YJ, Tian JW. The value of strain ratio in differential diagnosis of thyroid solid nodules. Eur J Radiol. 2012;81(2):286-91.

Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Thyroid. 2009;19(11):1159-65.

Trimboli P, Guglielmi R, Monti S, Misischi I, Graziano F, Nasrollah N, et al. Ultrasound sensitivity for thyroid malignancy is increased by real-time elastography: a prospective multicenter study. J Clin Endocrinol Metab 2012;97(12):4524–30.

Asteria C, Giovanardi A, Pizzocaro A, Cozzaglio L, Morabito A, Somalvico F, et al. USelastography in the differential diagnosis of benign and malignant thyroid nodules. Thyroid 2008;18(5):523–31.

PERFORMA

Hosp. Reg. No.: _____ Date:_____
Name: _____ _____ Age: __(years) Duration of Symptoms: _____
(Months)

GENDER Male o Female o RESIDENCE STATUS Urban o Rural o OCCUPATIONAL STATUS Employed o Unemployed o FAMILY MONTHLY INCOME	
Lower Income Group (Monthly Income ≤ 20,000)	o
Lower Middle Income Group (Monthly Income 20,0001 – 35,000	o
Middle Income Group (Monthly Income 35,0001 – 45,000)	o
Upper Middle Income Group (Monthly Income 45,0001 – 55,000	o
Upper Income Group (Monthly Income ≥55,001	o

MALIGNANCY OF THYROID NODULE			
SONOELASTOGRAPHY			
Positive	o	Negative	o
HISTOPATHOLOGY			
Positive	o	Negative	o

FIGURE 1:

A strategy for the initial evaluation of a nodule on the thyroid in a patient. (Adapted from Cooper Digital. The American the Thyroid Organization has amended its care recommendations for individuals with thyroid nodules and differentiated thyroid cancer. 2009; Thyroid 19(11):1167–214; accessed with permission. Calcitonin is a sensitive marker for MTC surveillance and prognosis, as well as detecting C-cell hyperplasia. MTC was found to be extremely sensitive to doses less than 10 pg/mL, and when Calcitonin levels exceeding 100 pg/mL, pentagastrin stimulation increased specificity. Despite being demonstrated to be a valuable and cost-effective tool in the thyroid nodule evaluation methodology, calcitonin screening is underutilized in the United States, owing in part to the low prevalence of medullary thyroid cancer and the lack of availability of pentagastrin. [33].

Serum thyroglobulin, a marker of Iodine consumption, and thyroid gland size cannot predict the frequency of thyroid cancer in nodular thyroid disease. As a result, it is not recommended to measure it regularly during the first diagnosis of a thyroid nodule. [33].

FIGURE 2:

This ultrasound of a thyroid nodule (arrowheads) with several fine punctuate echogenicities (arrow) and no comet-tail artifact indicates a high risk of cancer. PTC was verified with surgery and FNA. (Adapted from Frates MC). Radiology 2005; 237:794-800; reprinted with permission from the Society of Radiologists' Ultrasound consensus conference statement on the therapy of thyroid nodules found in the United States.

FIGURE 3:

A thyroid nodule with substantial internal vascularity on Doppler Color Ultrasound (Figure 4) may be cancerous. Histology confirmed the existence of PTC. (From the Society of Radiologists in Ultrasound consensus conference statement, Frates MC. Management of thyroid nodules identified during US; Radiology 2005;237:794-800; with permission.)

FIGURE 4:

Arrowheads indicate a cystic thyroid nodule on a US picture. (Taken from Frates MC. Treatment of thyroid nodules found in the United States: consensus statement from the Society of Radiologists in Ultrasound. 2005; 237:794–800; published by permission in Radiology.)

Both the quantity and size of nodules do not indicate malignancy since, in the presence of questionable US findings, a nodule less than 1 cm is just as likely as a larger one to contain cancer cells. The use of a random size as a cutoff for the likelihood of malignancy, as well as risk stratification in a multinodular goiter based on the "dominant" nodule, has fallen out of favor [37]

US examination of cervical lymph nodes demonstrates important indicators of a malignant etiology include concomitant ipsilateral thyroid nodules, round shape, enhanced vascularity, Cystic changes and micro calcifications. An additional extracapsular growth, such as infiltration of the thyroid capsule, per thyroidal muscle invasion, or extension of the recurrent laryngeal nerve, is a strong indication of malignancy. [37-38].

Given the low aggressiveness and slow progression of the majority of thyroid malignancies, screening for thyroid nodules with ultrasound or any other sort of imaging examination is not suggested for the general public. According to the current ATA rules. [17], diagnostic thyroid sonography should only be carried out in patients who have thyroid nodules, whether they are known or suspected, or who have risk factors.

Although they are not recommended for regular thyroid nodule examination, other diagnostic imaging modalities like MRIs and CT scans can be useful in determining nodule size, the substernal extension of a cystic goiter, and tracheal compression.[32].

FIGURE: 5

A system for tracking harmless thyroid nodules.

The definitions of nodule growth and the size thresholds for repeating a FNA are not commonly accepted. However, a number of researchers propose that a realistic and safe criterion of 50% be used Nodule volume development, or more than a 20% increase in at least two dimensions of a solid nodule, or the solid portion

of a mixed cystic-solid nodule [59]. The ATA website has an online calculator that can be utilized to calculate the change in volume of a thyroid nodule based on its serial dimensions. (http://www.thyroid.org/professionals/calculators/CINV.php). Nodule proliferation is not usually indicative of malignancy. Even though it is a sign to get a second biopsy. Since palpation-guided FNA has a higher false-negative rate than US-guided FNA, repeated FNA biopsies should be carried out under US direction. The accuracy of the initial diagnosis was shown to be high (98%) in a recent retrospective examination evaluating the utility of repeated FNAs of benign thyroid nodules [60].
If there is no discernible nodule growth during subsequent US visits, a three- to five-year follow-up period would be appropriate. [17].

TABLE # 1
DESCRIPTIVE STATISTICS OF AGE n=174
TABLE # 2
DESCRIPTIVE STATISTICS FOR DURATION OF SYMPTOMS n=174

FIGURE#8
FREQUENCY OF RESIDENTIAL STATUS n=174
FIGURE#9
FREQUENCY OF OCCUPATIONAL STATUS n=174
TABLE # 3
FREQUENCY OF FAMILY MONTHLY INCOME n=174
FIGURE # 10
FREQUENCY OF MALIGNANCY OF THYROID NODULE ON SONOELASTOGRAPHY n=174

FIGURE # 11
FREQUENCY OF MALIGNANCY OF THYROID NODULE ON HISTOPATHOLOGY n=174
TABLE # 4
DIAGNOSTIC ACCURACY OF SONOELASTOGRAPHY BY USING HISTOPATHOLOGY AS GOLD STANDARD n=174

The
Research of Medical Science Review

TABLE # 5
STRATIFICATION OF AGE GROUP WITH RESPECT TO SONOELASTOGRAPHY n=174
TABLE # 6
STRATIFICATION OF GENDER WITH RESPECT TO SONOELASTOGRAPHY n=174

TABLE # 7
STRATIFICATION FOR DURATION OF SYMPTOMS WITH RESPECT TO SONOELASTOGRAPHY n=174
TABLE # 8
STRATIFICATION OF RESIDENTIAL STATUS WITH RESPECT TO SONOELASTOGRAPHY n=174

TABLE # 9
STRATIFICATION OF OCCUPATIONAL STATUS WITH RESPECT TO SONOELASTOGRAPHY n=174
Tables:

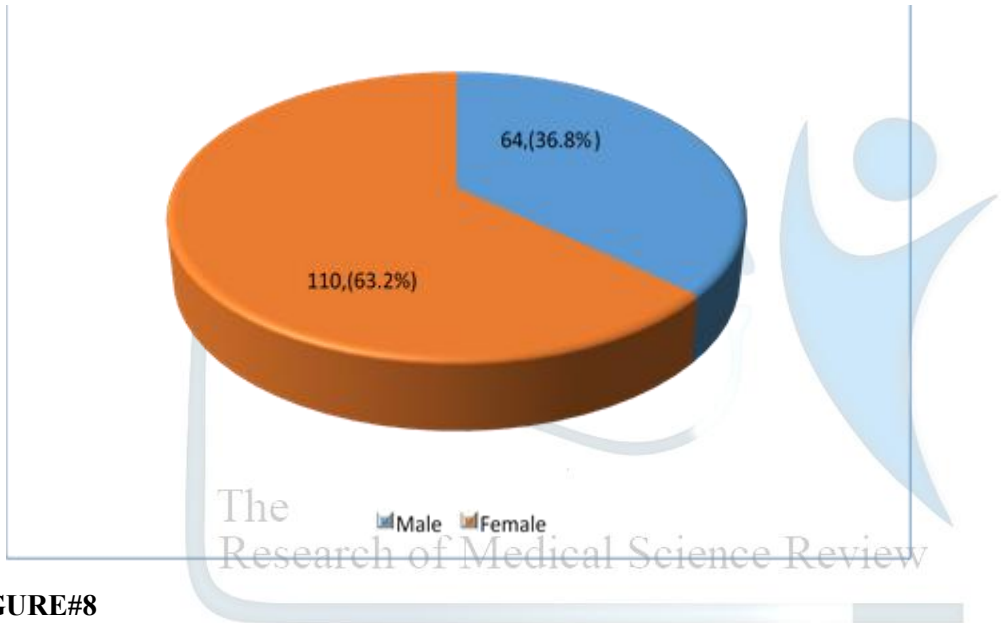
MEAN	37.7 (Years)
STANDARD DEVIATION	7.2
95% CONFIDENCE INTERVAL	36.62…….38.77
MINIMUM	20
MAXIMUM	60

RANGE	40

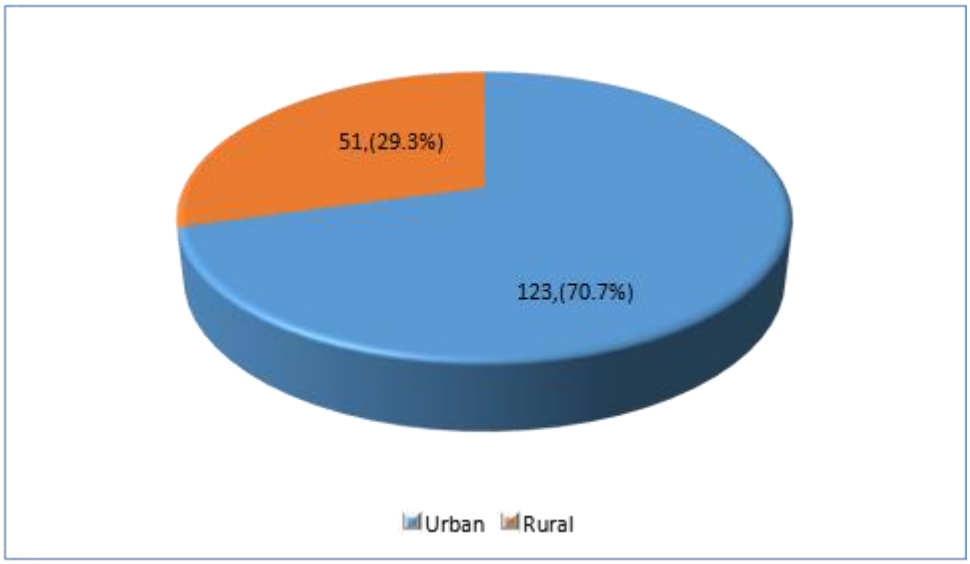
TABLE # 1
DESCRIPTIVE STATISTICS OF AGE n=174

MEAN	6.5 (Months)
STANDARD DEVIATION	2.4
95% CONFIDENCE INTERVAL	6.14…….6.85
MINIMUM	1
MAXIMUM	24
RANGE	23

TABLE # 2
DESCRIPTIVE STATISTICS FOR DURATION OF SYMPTOMS
n=174



FIGURE#8
FREQUENCY OF RESIDENTIAL STATUS n=174



FIGURE#9
FREQUENCY OF OCCUPATIONAL STATUS n=174

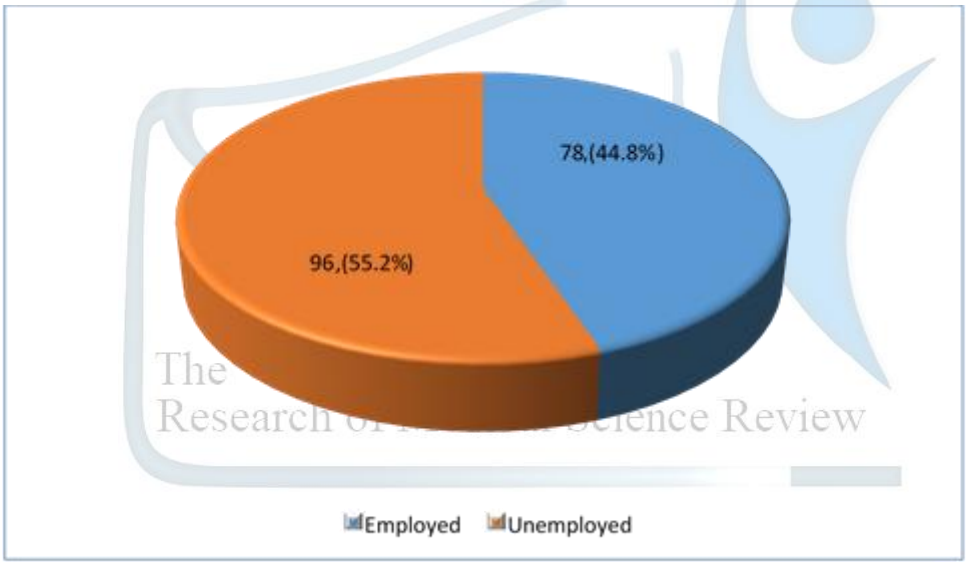


TABLE # 3
FREQUENCY OF FAMILY MONTHLY INCOME n=174

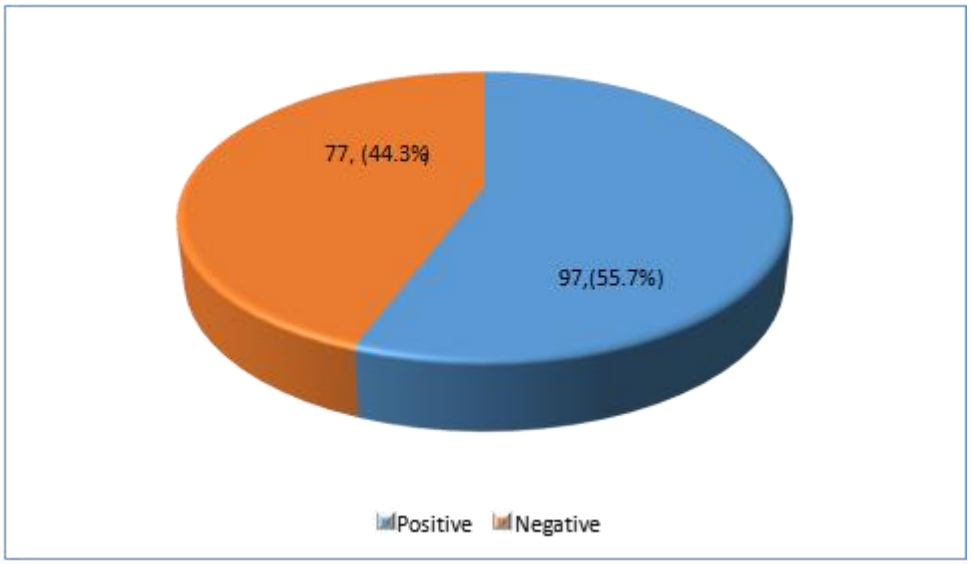


FIGURE # 10
FREQUENCY OF MALIGNANCY OF THYROID NODULE ON SONOELASTOGRAPHY n=174

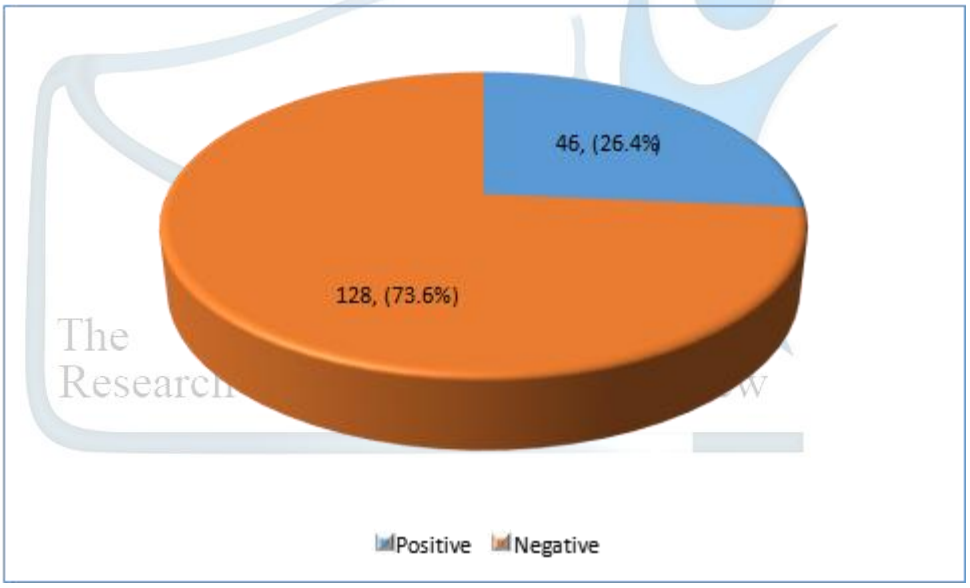


FIGURE # 11
FREQUENCY OF MALIGNANCY OF THYROID NODULE ON HISTOPATHOLOGY n=174

TABLE # 4
DIAGNOSTIC ACCURACY OF SONOELASTOGRAPHY BY USING HISTOPATHOLOGY AS GOLD STANDARD n=174

SONOELASTOGRAPHY	HISTOPATHOLOGY (GOLD STANDARD)	
	POSITIVE	NEGATIVE
POSITIVE	True positive(a) 39	False positive(b) 44
NEGATIVE	False negative(c) 7	True negative (d) 84
Total	a + c	b + d

	46	128

				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.8478	84.78	0.7440	0.9516
Specificity	d/ (b + d)	0.6563	65.63	0.5740	0.7385
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.2644	26.44	0.1988	0.3299
Positive Predictive value	a/ (a +b)	0.4699	46.99	0.3625	0.5773
Negative Predictive value	d/ (c+ d)	0.9231	92.31	0.8683	0.9778
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.7069	70.69	0.6393	0.7745

TABLE # 5
STRATIFICATION OF AGE GROUP WITH RESPECT TO SONOELASTOGRAPHY n=174

FOR AGE GROUP 20---40 (n=111)				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.8000	80.00	0.6432	0.9568
Specificity	d/ (b + d)	0.7442	74.42	0.6520	0.8364
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.2252	22.52	0.1475	0.3029
Positive Predictive value	a/ (a +b)	0.4762	47.62	0.3251	0.6272
Negative Predictive value	d/ (c+ d)	0.9275	92.75	0.8664	0.9887
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.7568	75.68	0.6769	0.8366

FOR AGE GROUP > 40 (n=63)				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.9048	90.48	0.7792	1.0303
Specificity	d/ (b + d)	0.4762	47.62	0.3251	0.6272
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.3333	33.33	0.2169	0.4497
Positive Predictive value	a/ (a +b)	0.4634	46.34	0.3108	0.6161
Negative Predictive value	d/ (c+ d)	0.9091	90.91	0.7890	1.0292
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.6190	61.90	0.4991	0.7390

TABLE # 6: STRATIFICATION OF GENDER WITH RESPECT TO SONOELASTOGRAPHY n=174

GENDER	HISTOPATHOLOGY (GOLD STANDARD)	
	POSITIVE	NEGATIVE

Male (n= 64)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 11	False positive (b) 19
		NEGATIVE	False negative(c) 1	True negative (d) 33
Female (n= 110)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 28	False positive (b) 25
		NEGATIVE	False negative(c) 6	True negative (d) 51

FOR GENDER MALE (n=64)				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.9167	91.67	0.7603	1.0730
Specificity	d/ (b + d)	0.6346	63.46	0.5037	0.7655
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.1875	18.75	0.0919	0.2831
Positive Predictive value	a/ (a +b)	0.3667	36.67	0.1942	0.5391
Negative Predictive value	d/ (c+ d)	0.9706	97.06	0.9138	1.0274
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.6875	68.75	0.5739	0.8011
Positive Predictive value	a/ (a +b)	0.5283	52.83	0.3939	0.6627
Negative Predictive value	d/ (c+ d)	0.8947	89.47	0.8151	0.9744
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.7182	71.82	0.6341	0.8023

TABLE # 7

STRATIFICATION FOR DURATION OF SYMPTOMS WITH RESPECT TO SONOELASTOGRAPHY n=174

DURATION [In Months]			HISTOPATHOLOGY (GOLD STANDARD)	
			POSITIVE	NEGATIVE
1 - 6 (n= 92)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 23	False positive (b) 20
		NEGATIVE	False negative(c) 2	True negative (d) 47
>6 (n=82)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 16	False positive (b) 24
		NEGATIVE	False negative(c) 5	True negative (d) 37

FOR DURATION 0---6 (n=92)				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.9200	92.00	0.8137	1.0263
Specificity	d/ (b + d)	0.5919	59.19	0.5919	0.8111
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.2717	27.17	0.1808	0.3626
Positive Predictive value	a/ (a +b)	0.5349	53.49	0.3858	0.6840
Negative Predictive value	d/ (c+ d)	0.9592	95.92	0.9038	1.0146
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.7609	76.09	0.6737	0.8480

FOR	DURATION >6 (n=82)	95% Confidence Interval	
		Lower	Upper

Sensitivity	a/ (a + c)	0.7619	76.19	0.5797	0.9441
Specificity	d/ (b + d)	0.6066	60.66	0.4840	0.7292
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.2561	25.61	0.1616	0.3506
Positive Predictive value	a/ (a +b)	0.4000	40.00	0.2482	0.5518
Negative Predictive value	d/ (c+ d)	0.8810	88.10	0.7830	0.9789
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.6463	64.63	0.5429	0.7498

TABLE # 8

STRATIFICATION OF RESIDENTIAL STATUS WITH RESPECT TO SONOELASTOGRAPHY n=174

RESIDENTIAL STATUS			HISTOPATHOLOGY (GOLD STANDARD)	
			POSITIVE	NEGATIVE
Urban (n= 123)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 29	False positive (b) 31
		NEGATIVE	False negative(c) 6	True negative (d) 57
Rural (n=51)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 10	False positive (b) 24
		NEGATIVE	False negative(c) 1	True negative (d) 16

FOR RESIDENTIAL STATUS URBAN (n=123)				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.8286	82.86	0.7037	0.9534
Specificity	d/ (b + d)	0.6477	64.77	0.5479	0.7475
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.2846	28.46	0.2048	0.3643
Positive Predictive value	a/ (a +b)	0.4833	48.33	0.3569	0.6098
Negative Predictive value	d/ (c+ d)	0.9048	90.48	0.8323	0.9772
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.6992	69.92	0.6181	0.7802

FOR RESIDENTIAL STATUS RURAL (n=51)				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.9091	90.91	0.7392	1.0790
Specificity	d/ (b + d)	0.4000	40.00	0.2482	0.5518
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.2157	21.57	0.1028	0.3286
Positive Predictive value	a/ (a +b)	0.2941	29.41	0.1410	0.4473
Negative Predictive value	d/ (c+ d)	0.9412	94.12	0.8293	1.0530
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.5098	50.98	0.3726	0.6470

TABLE # 9

STRATIFICATION OF OCCUPATIONAL STATUS WITH RESPECT TO SONOELASTOGRAPHY n=174

OCCUPATIONAL STATUS			HISTOPATHOLOGY (GOLD STANDARD)	
			POSITIVE	NEGATIVE
Employed (n=78)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 21	False positive (b) 16
		NEGATIVE	False negative(c) 3	True negative (d) 38
Unemployed (n=96)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 18	False positive (b) 28
		NEGATIVE	False negative(c) 4	True negative (d) 46

FOR OCCUPATIONAL STATUS EMPLOYED (n=78)				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.8750	87.50	0.7427	1.0073
Specificity	d/ (b + d)	0.7037	70.37	0.5819	0.8255
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.3077	30.77	0.2053	0.4101
Positive Predictive value	a/ (a +b)	0.5676	56.76	0.4079	0.7272
Negative Predictive value	d/ (c+ d)	0.9268	92.68	0.8471	1.0065
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.7564	75.64	0.6611	0.8517

The
Research of Medical Science Review

FOR OCCUPATIONAL STATUS UNEMPLOYED (n=96)				95% Confidence Interval	
				Lower	Upper
Sensitivity	a/ (a + c)	0.8182	81.82	0.6570	0.9794
Specificity	d/ (b + d)	0.6216	62.16	0.5111	0.7321
Prevalence of disease	(a+ c)/ (a+ b+ c+ d)	0.2292	22.92	0.1451	0.3132
Positive Predictive value	a/ (a +b)	0.3913	39.13	0.2503	0.9952
Negative Predictive value	d/ (c+ d)	0.9200	92.00	0.8448	0.9952
Overall accuracy**	(a+ d)/ (a+ b+ c+ d)	0.6667	66.67	0.5724	0.7610

AGE GROUP [In Years]			HISTOPATHOLOGY (GOLD STANDARD)	
			POSITIVE	NEGATIVE
20 --- 40 (n= 111)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 20	False positive (b) 22
		NEGATIVE	False negative(c) 5	True negative (d) 64
> 40 (n= 53)	SONOELASTOGRAPHY	POSITIVE	True positive(a) 19	False positive (b) 22
		NEGATIVE	False negative(c) 2	True negative (d) 20

FAMILY MONTHLY INCOME	FREQUENCY	PERCENTAGE
Lower Income Group	19	11.0%
Lower Middle-Income Group	65	37.3%
Middle-Income Group	42	24.1%
Upper-Middle-Income Group	28	16.1%
Upper-Income Group	20	11.5%

The Research of Medical Science Review

FIGURE WITH LEGEND.

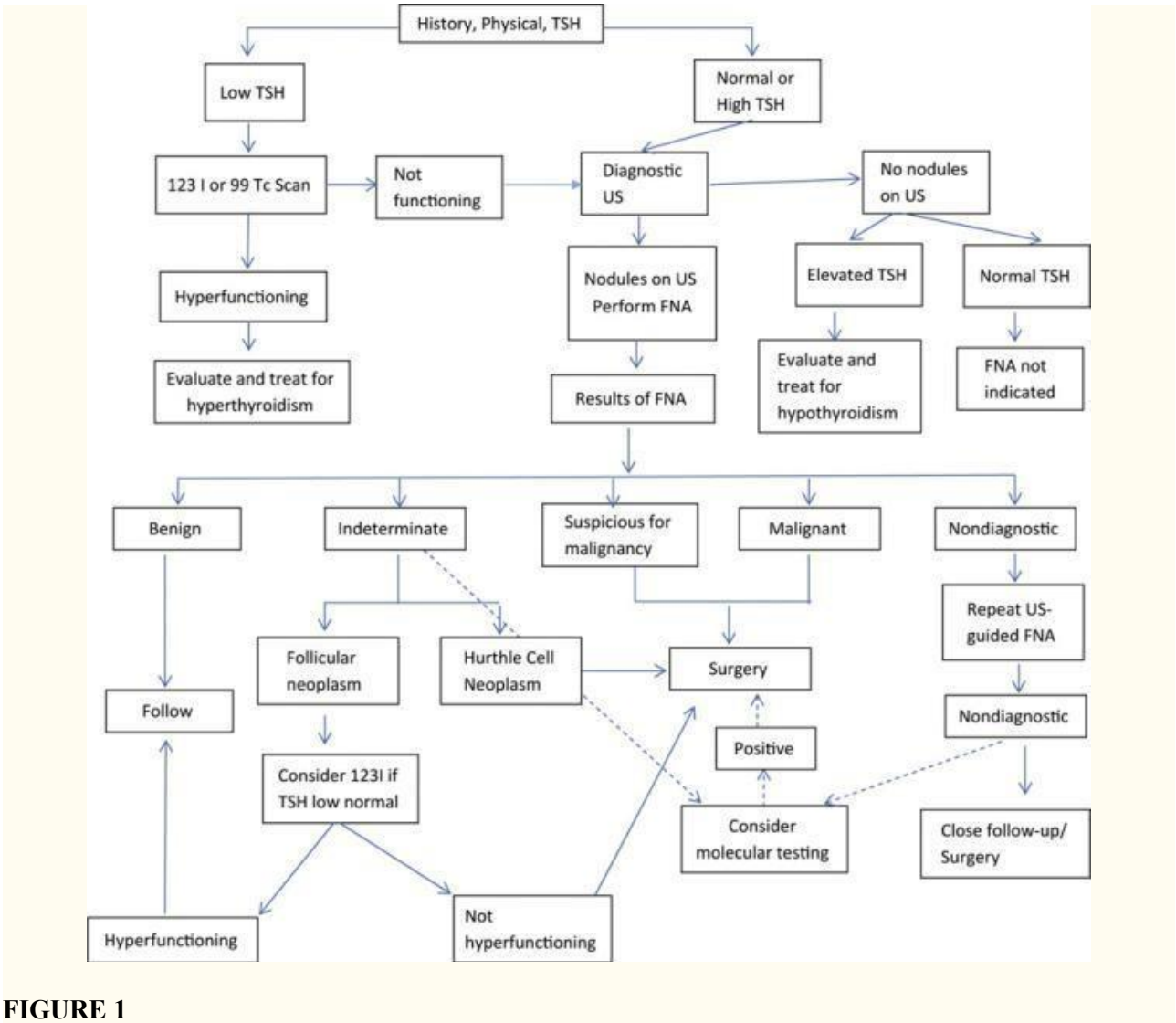


FIGURE 1

the United States, owing in part to the low prevalence of medullary thyroid cancer and the lack of availability of pentagastrin. [33].

Serum thyroglobulin, a marker of Iodine consumption, and thyroid gland size cannot predict the frequency of thyroid cancer in nodular thyroid disease. As a result, it is not recommended to measure it regularly during the first diagnosis of a thyroid nodule. [33].

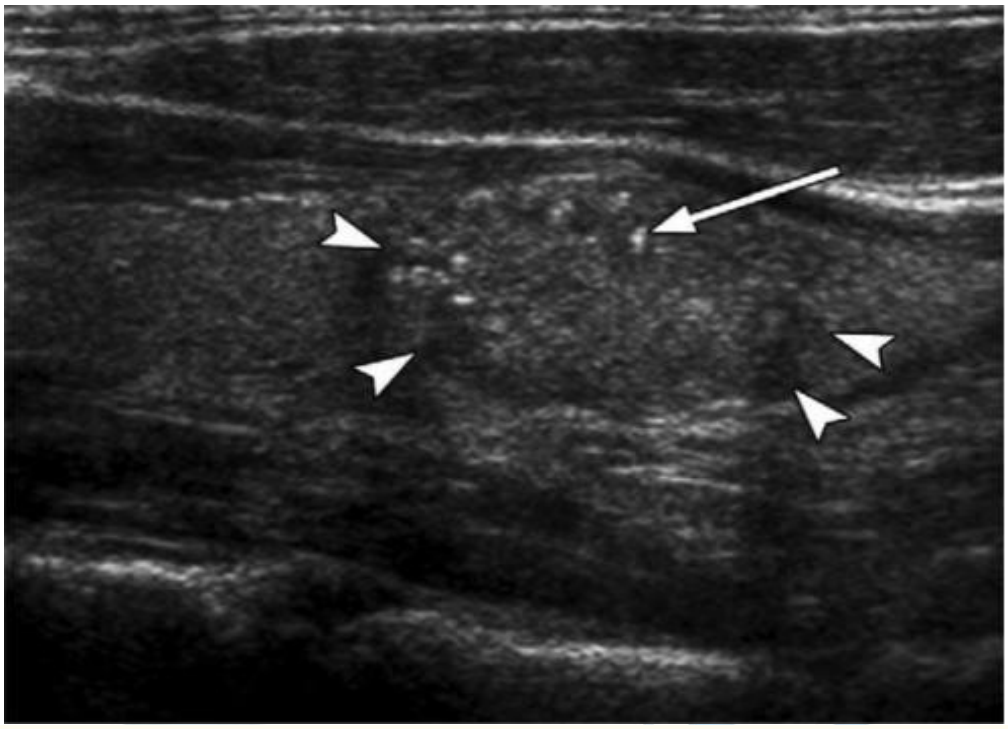
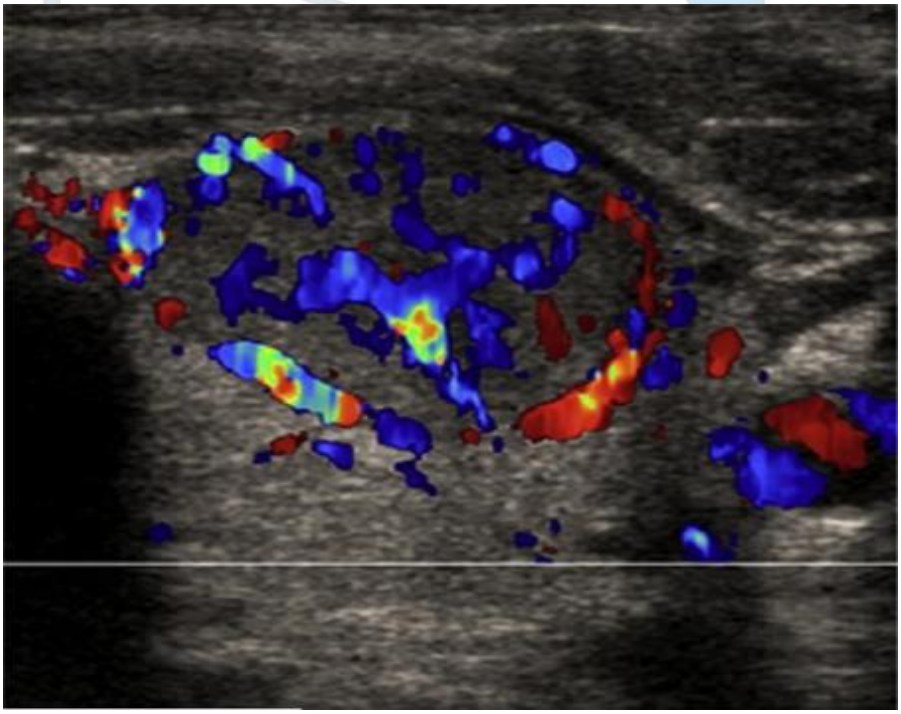


FIGURE 2
This ultrasound of a thyroid nodule (arrowheads) with several fine punctuate echogenicities (arrow) and no comet-tail artifact indicates a high risk of cancer. PTC was verified with surgery and FNA. (Adapted from Frates MC). Radiology 2005; 237:794-800; reprinted with permission from t



The Society of Radiologists' Ultrasound consensus conference statement on the therapy of thyroid nodules found in the United States.

FIGURE 3

A thyroid nodule with substantial internal vascularity on Doppler Color Ultrasound (Figure 4) may be cancerous. Histology confirmed the existence of PTC. (From the Society of Radiologists in Ultrasound consensus conference statement, Frates MC. Management of thyroid nodules identified during US; Radiology 2005;237:794-800; with permission.)

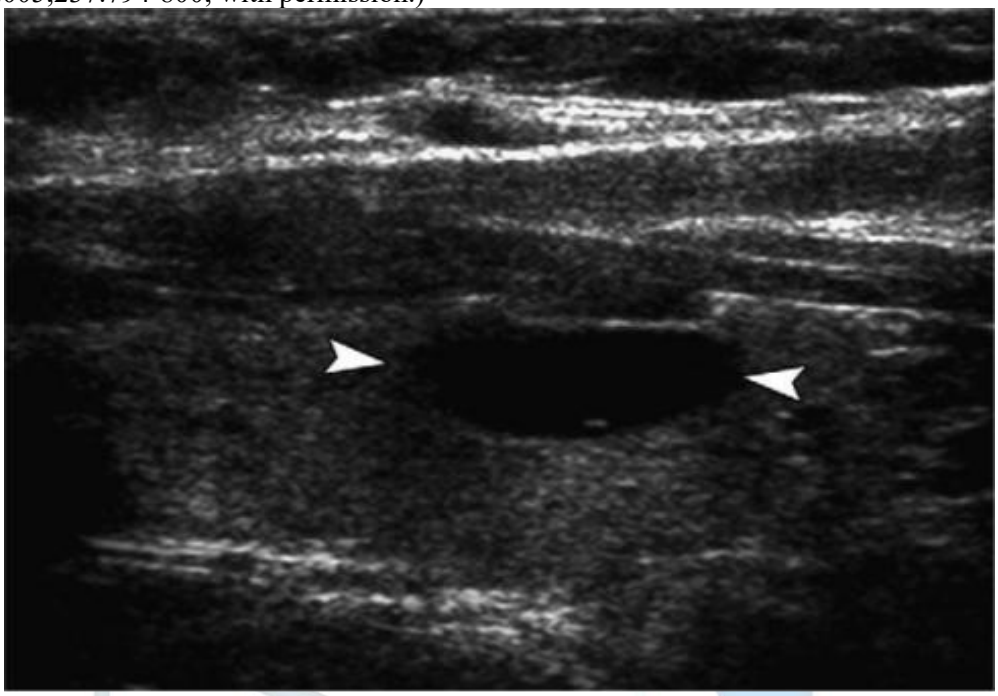


FIGURE 4:

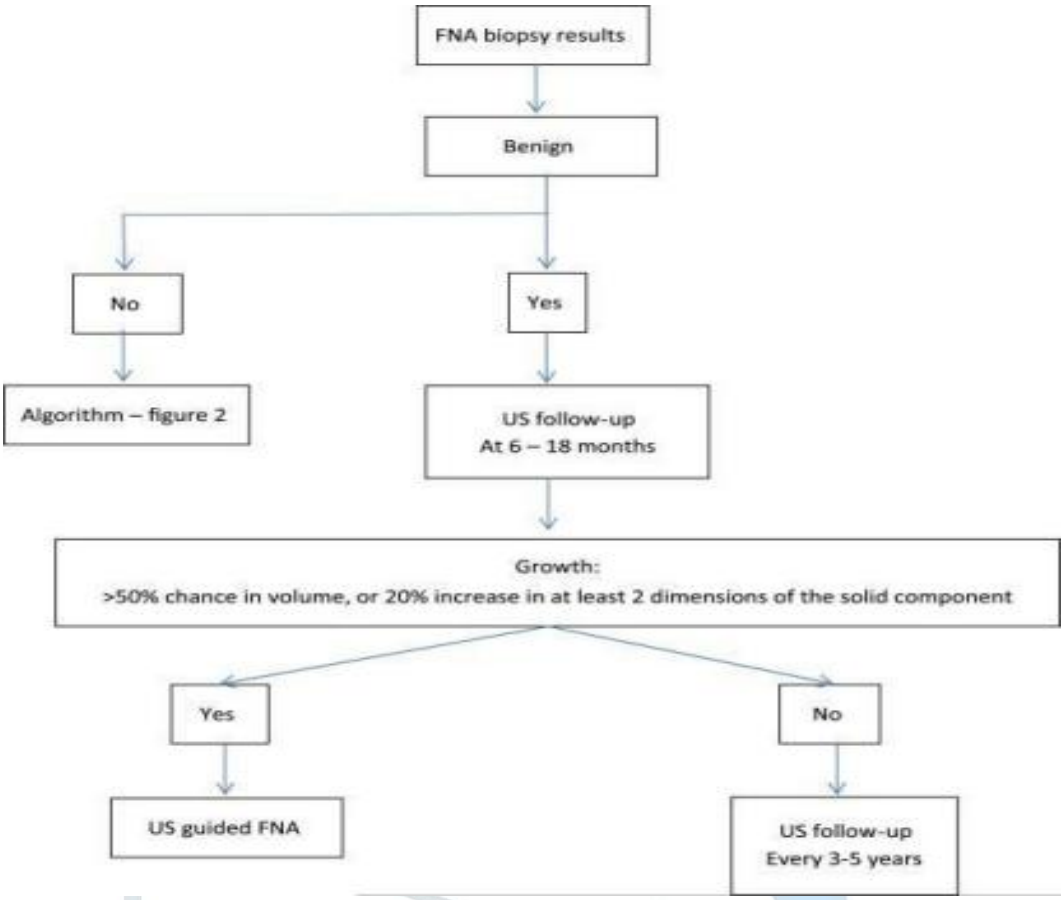
Arrowheads indicate a cystic thyroid nodule on a US picture. (Taken from Frates MC. Treatment of thyroid nodules found in the United States: consensus statement from the Society of Radiologists in Ultrasound. 2005; 237:794–800; published by permission in Radiology.)

Both the quantity and size of nodules do not indicate malignancy since, in the presence of questionable US findings, a nodule less than 1 cm is just as likely as a larger one to contain cancer cells. The use of a random size as a cutoff for the likelihood of malignancy, as well as risk stratification in a multinodular goiter based on the "dominant" nodule, has fallen out of favor [37]

US examination of cervical lymph nodes demonstrates important indicators of a malignant etiology include concomitant ipsilateral thyroid nodules, round shape, enhanced vascularity, Cystic changes and microcalcifications. An additional extracapsular growth, such as infiltration of the thyroid capsule, perithyroidal muscle invasion, or extension of the recurrent laryngeal nerve, is a strong indication of malignancy. [37-38].

Given the low aggressiveness and slow progression of the majority of thyroid malignancies, screening for thyroid nodules with ultrasound or any other sort of imaging examination is not suggested for the general public. According to the current ATA rules. [17], diagnostic thyroid sonography should only be carried out in patients who have thyroid nodules, whether they are known or suspected, or who have risk factors.

Although they are not recommended for regular thyroid nodule examination, other diagnostic imaging modalities like MRIs and CT scans can be useful in determining nodule size, the substernal extension of a cystic goitre, and tracheal compression.[32].



A system for tracking harmless thyroid nodules.

The definitions of nodule growth and the size thresholds for repeating a FNA are not commonly accepted. However, a number of researchers propose that a realistic and safe criterion of 50% be used Nodule volume development, or more than a 20% increase in at least two dimensions of a solid nodule, or the solid portion of a mixed cystic-solid nodule [59]. The ATA website has an online calculator that can be utilized to calculate the change in volume of a thyroid nodule based on its serial dimensions. (http://www.thyroid.org/professionals/calculators/CINV.php). Nodule proliferation is not usually indicative of malignancy. Even though it is a sign to get a second biopsy. Since palpation-guided FNA has a higher false-negative rate than US-guided FNA, repeated FNA biopsies should be carried out under US direction. The accuracy of the initial diagnosis was shown to be high (98%) in a recent retrospective examination evaluating the utility of repeated FNAs of benign thyroid nodules [60].

If there is no discernible nodule growth during subsequent US visits, a three- to five-year follow-up period would be appropriate. [17].