

# **EVALUATION OF RISK FACTORS FOR MALIGNANCY IN A SOLITARY THYROID NODULE**

*Thesis*

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Degree in General Surgery*

*By*

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# *List of Contents*

<b>Title</b>	<b>Page No.</b>
List of Tables .....	i
List of Figures.....	iii
List of Abbreviations .....	v
Introduction .....	1
Aim of the Work.....	3
<b>Review of Literature</b>	
• Surgical Anatomy and Physiology of the Thyroid Gland.....	4
• Pathology of nodular goiter and thyroid neoplasms .....	15
• Diagnostic Approach of the Solitary Thyroid Nodule (STN).....	30
• Management of Thyroid Malignancies.....	60
Patients and Methods.....	85
Results .....	91
Discussion.....	107
Summary.....	113
Conclusion.....	116
References .....	117
Arabic Summary.....	

## *List of Tables*

Table No.	Title	Page No.
<b>Table (1):</b>	Physiologic effects of Thyroid hormones.....	14
<b>Table (2):</b>	Familial Thyroid Cancer Syndromes .....	17
<b>Table (3):</b>	US features associated with Benign or Malignant probability of STNs .....	41
<b>Table (4):</b>	US & Clinical features of STNs and FNAB Recommendations .....	42
<b>Table (5):</b>	US features, Estimated risk of malignancy, and FNA cutoffs for STN Sonographic patterns.....	54
<b>Table (6):</b>	ATA Criteria for FNAB of a Thyroid Nodule .....	55
<b>Table (7):</b>	AACE Classification for Cytologic Diagnosis and Management Recommendations. (ATA 2015 Guidelines).....	55
<b>Table (8):</b>	The Bethesda System. Description, Risk, and Recommendation.....	56
<b>Table (9):</b>	Familial Thyroid Cancer Syndromes.....	64
<b>Table (10):</b>	Clinical and Sonographic Features of STN Malignancy.....	69
<b>Table (11):</b>	Indications and Definition of the Extent of Resection in different types of Thyroidectomy .....	78
<b>Table (12):</b>	Comparison between pre-op. data and post-op. HP regarding Age.....	94
<b>Table (13):</b>	Comparison between pre-op. data and post-op. HP regarding Gender.....	95
<b>Table (14):</b>	Comparison between pre-op. data and post-op. histopathology regarding residence.....	96
<b>Table (15):</b>	Comparison between pre-op. data and post-op. HP as regards special habits.....	97
<b>Table (16):</b>	Comparison between pre-op. data and post-op. HP as regards the Main Complaint.....	98
<b>Table (17):</b>	Comparison between pre-op. data and post-op. HP as regards Other Complaints .....	99
<b>Table (18):</b>	Comparison between pre-op. data and post-op. HP regarding Medical History.....	100
<b>Table (19):</b>	Comparison between pre-op. data and post-op. HP regarding family history of thyroid disease.....	101

## *List of Tables (Cont.)*

Table No.	Title	Page No.
<b>Table (20):</b>	Comparison between Nodule Dimensions on US and postoperative histopathology.....	102
<b>Table (21):</b>	Measurement of agreement between Nodule Echogenicity and Postoperative Histopathology.....	104
<b>Table (22):</b>	Measurement of Agreement between Local Examination for <i>Cervical Lymphadenopathy</i> and post-op. HP.....	104
<b>Table (23):</b>	Measurement of agreement between FNAC and postoperative histopathology results. ....	105

## *List of Figures*

Fig. No.	Title	Page No.
<b>Figure (1):</b>	Anatomy of the Thyroid Gland.....	4
<b>Figure (2):</b>	Relations of the Thyroid .....	5
<b>Figure (3):</b>	Anatomy of the Thyroid Gland (all muscles cut) .....	6
<b>Figure (4):</b>	Arterial Supply of the Thyroid.....	7
<b>Figure (5):</b>	Relationship of the RLN to ITA branches .....	8
<b>Figure (6):</b>	Venous drainage of the Thyroid .....	8
<b>Figure (7):</b>	Lymphatic drainage of the thyroid compartment with anterior and lateral neck regions .....	9
<b>Figure (8):</b>	RLNs in the chest and neck .....	10
<b>Figure (9):</b>	<i>A:</i> EBSLN descends superficial to the IC muscle. <i>B:</i> EBSLN pierces the IC muscle (arrow). <i>C:</i> EBSLN runs deep to the IC muscle .....	11
<b>Figure (10):</b>	FNAC specimen demonstrating chronic lymphocytic thyroiditis .....	20
<b>Figure (11):</b>	Sub-acute Thyroiditis.....	21
<b>Figure (12):</b>	A HP section from a case of MNG .....	22
<b>Figure (13):</b>	US and HP appearance of different benign and malignant goiters.....	23
<b>Figure (14):</b>	The frequency of occurrence of different pathologic types of thyroid malignancy.....	24
<b>Figure (15):</b>	PTC, Gross specimen sectioned.....	26
<b>Figure (16):</b>	PTC showing the diagnostic feature Orphan Annie eye nuclei.....	27
<b>Figure (17):</b>	FTC .....	27
<b>Figure (18):</b>	MTC .....	29
<b>Figure (19):</b>	A Solitary Thyroid Nodule (arrow) in a 16-year-old girl .....	30
<b>Figure (20):</b>	US patterns in benign and malignant STNs.....	42
<b>Figure (21):</b>	A&C: Microcalcifications, A&D: Solid Nodules.....	43
<b>Figure (22):</b>	Image of a STN ( <i>arrowheads</i> ) containing multiple punctuate echogenecities ( <i>arrow</i> ) without comet-tail artifact indicating high suspicion for malignancy.....	44
<b>Figure (23):</b>	Color Doppler US of a thyroid nodule.....	46
<b>Figure (24):</b>	Benign Findings in STNs.....	47
<b>Figure (25):</b>	A benign 1.2 cm spongiform thyroid nodule (marked) in an 80-year-old patient).....	47

## *List of Figures (Cont.)*

Fig. No.	Title	Page No.
<b>Figure (26):</b>	Tc <sup>99m</sup> -pertechnetate and MIBI scan.....	52
<b>Figure (27):</b>	Axial CT images of the neck at the level of the tongue base .....	52
<b>Figure (28):</b>	Schema of key pathways in the development and progression of Thyroid Cancer .....	63
<b>Figure (29):</b>	A 3 cm nodule showing microcalcifications and increased peripheral vascularity.....	70
<b>Figure (30):</b>	<i>Left</i> , Halo Sign and <i>Right</i> , Peripheral vascular flow pattern .....	70
<b>Figure (31):</b>	<i>Left</i> , two examples of perinodular hypervascularity in two patients. <i>Right</i> , A hypoechoic nodule with intranodular vascularity .....	71
<b>Figure (32):</b>	Examples of hypoechoic ( <i>A</i> ), isoechoic ( <i>B</i> ), and hyperechoic ( <i>C</i> ) thyroid nodules.....	72
<b>Figure (33):</b>	Typical findings noted on Thyroid US .....	72
<b>Figure (34):</b>	Management of Neck Lymph Nodes .....	81
<b>Figure (35):</b>	Bar chart representing comparison between pre-op.....	94
<b>Figure (36):</b>	Bar chart representing comparison between pre-op. data and post-op. HP as regards gender.....	95
<b>Figure (37):</b>	Bar chart representing comparison between pre-op. data and post-op. HP as regards residence.....	96
<b>Figure (38):</b>	Bar chart representing comparison between pre-op. data and post-op. HP as regards special habits.....	97
<b>Figure (39):</b>	Bar chart representing comparison between pre-op. data and post-op. HP regards the Main Complaint.....	98
<b>Figure (40):</b>	Bar chart representing comparison between pre-op. data and post-op. HP regards other complaints.....	99
<b>Figure (41):</b>	Bar chart representing comparison between pre-op. data and post-op. HP regards medical history.....	101
<b>Figure (42):</b>	Bar chart representing comparison between pre-op.....	102
<b>Figure (43):</b>	Bar chart representing comparison between pre-op.....	103

## *List of Abbreviations*

<b>Abb.</b>	<b>Full term</b>
AACE .....	American Association of Clinical Endocrinologists; ATA, American Thyroid Association; ATC,
ANOVA .....	Analysis of variance
AP/T .....	Anteroposterior/transverse diameter
APC .....	Annual percentage change
ASIRW .....	Age-standardized incidence rate by world population
ATA .....	American Thyroid Association
ATC .....	Anaplastic thyroid carcinoma
AUS .....	Atypia of undetermined significance
B .....	PBs,
BI-RADS .....	Breast imaging reporting and data system
BRAF .....	B-Raf proto-oncogene, serine/threonine kinase
BRAF, BRAF .....	Protein (oncogene)
BST .....	Bilateral subtotal thyroidectomy,
Camp .....	Cyclic adenosine monophosphate
CCH .....	C-Cell hyperplasia
CEA .....	Carcinoembryonic antigen
CI .....	Confidence Interval
CT .....	Computed tomography
Ct .....	Calcitonin
CVPTC .....	Classical variant of papillary thyroid carcinoma
DM .....	Distant Metastasis
DO .....	Dunhill operation,
DTC .....	Differentiated thyroid carcinoma
E2 .....	Estradiol
EANM .....	European Association of Nuclear Medicine
EDI .....	Electronic data interchange
EFC .....	Encapsulated follicular thyroid carcinoma

## *List of Abbreviations (Cont.)*

<b>Abb.</b>	<b>Full term</b>
EFVPTC .....	Encapsulated follicular variant of papillary thyroid carcinoma
EREs .....	Estrogen response elements
ERK .....	Extracellular signal-regulated kinase
ETE .....	Extra thyroidal extension
ETT .....	Endotracheal tube
FA .....	Follicular adenomas
FACS.....	Fluorescent activated cell sorter
factor-1.....	HLA-G, human leukocyte antigen
FC .....	Follicular thyroid cancer
FDG18 .....	Fluoro-deoxy-glucose
FLUS .....	Follicular lesion of undetermined significance
FMTC.....	Familial medullary thyroid cancer
FN .....	Follicular neoplasm
FNA .....	Fine needle aspiration
FNAB.....	Fine-needle aspiration biopsy
FNAC.....	Fine needle aspiration cytology
FTA .....	Follicular adenoma
FTC .....	Follicular thyroid carcinoma;
FVPTC.....	Follicular variant of papillary thyroid carcinoma
GEC .....	Afirma Gene Expression Classifier
GEE .....	Generalized estimated equations
GP .....	General practitioner
GPCR.....	G protein-coupled receptor
hCG, human .....	Chorionic gonadotropin
HIF-1 .....	Hypoxia inducible
HR.....	Hazard Ratio
HRT .....	Hormone replacement therapy,
HT .....	Hashimoto thyroiditis

## *List of Abbreviations (Cont.)*

<b>Abb.</b>	<b>Full term</b>
ICD.....	International classification of diseases
ICD-O.....	The International Classification of Diseases for Oncology
IFP .....	Increased interstitial fluid pressure
IJV .....	Internal jugular vein
IMRT.....	Intensity modulated radiotherapy
ITN.....	Incidental thyroid nodule
LNM.....	Lymph node metastases
MACIS .....	Metastases, Age at presentation, Completeness of surgical resection, Invasion (extrathyroidal), Size
MALT.....	Mucosa associated lymphoid tissue
MAPK .....	Mitogen-activated protein kinase
MDL.....	Minimum detection level
MDT.....	Multidisciplinary team
MEK.....	Mitogen-activated protein kinase kinase
MEN.....	Multiple endocrine neoplasia
MEN2.....	Multiple endocrine neoplasia type 2
MIBG .....	Metaiodobenzylguanidine
MKIs .....	Multi kinase inhibitors
MNG .....	Multinodular goiter
MRI.....	Magnetic resonance imaging
MRND.....	Modified radical neck dissection
MTC .....	Medullary thyroid cancer
MTD.....	Maximum tumor diameter
NCCN .....	National Comprehensive Cancer Network
NF- $\kappa$ .....	Nuclear factor-kappa
NHI .....	National Health Insurance
NHIS.....	National Health Insurance Service
NPV .....	Negative Predictive value

## *List of Abbreviations (Cont.)*

<b>Abb.</b>	<b>Full term</b>
OR.....	Odds Ratio
OS.....	Overall survival
PBDEs.....	Polybrominated diphenyl ether flame retardants
PDTC.....	Poorly differentiated thyroid carcinoma
PET.....	Positron emission tomography
PFS.....	Progression-free survival
PHEO.....	Pheochromocytoma
PHP.....	Primary hyperparathyroidism
PI3K.....	Phosphatidylinositol 3-kinase
PPV.....	Positive predictive value
PTC.....	Papillary thyroid carcinoma
PTH.....	Parathyroid hormone
PTMC.....	Papillary microcarcinoma
Ptnm.....	Pathologically staged according to Tumour size, Node metastases and distant Metastases
QIC.....	Quasi-likelihood under the independence criterion
QTc.....	Corrected QT interval (electrocardiogram)
RAI.....	Radioactive iodine
RAS.....	Ras proto-oncogene, GTPase
REC.....	research ethics committee
RET.....	Ret proto-oncogene
rhTSH.....	Recombinant human TSH
RIA.....	Radioimmunoassay
RLN.....	Recurrent laryngeal nerve
RR.....	Relative risk
RR-DTC.....	Radioiodine-refractory differentiated thyroid carcinoma
SAN.....	Spinal accessory nerve
SCM.....	Sternocleidomastoid muscle
SD.....	Standard deviation

## *List of Abbreviations (Cont.)*

<b>Abb.</b>	<b>Full term</b>
SEER .....	Surveillance, Epidemiology, and End Results Program
SFN.....	Suspicious for follicular neoplasm
SNG .....	Solitary nodular goiter,
SUSP.....	Suspicious for malignancy
T3.....	Triiodothyronine (liothyronine)
TC .....	Thyroid cancer
TCGA.....	The Cancer Genome Atlas
TFT .....	Thyroid function test
Tg .....	Thyroglobulin
TgAb .....	Anti-thyroglobulin antibodies
TI-RADS .....	Thyroid imaging reporting and data system
TKIs .....	Tyrosine kinase inhibitors
TKs.....	Tyrosine kinases
TNM.....	Staged according to Tumour size, Node and Metastases
TSG.....	Tumour-specific group
TSH.....	Thyroid-stimulating hormone
TSVPTC.....	Papillary thyroid carcinoma with trabecular-solid pattern of growth
TT.....	Total thyroidectomy
US .....	Ultrasonography
US .....	United States of America
UT.....	Unilateral thyroidectomy
WBS .....	Whole-body scan

## INTRODUCTION

**E**nlargements of the thyroid gland include a variety of disorders such as the endemic goiter of iodine deficiency, Primary hyperthyroidism (Graves' disease), STNs, MNGs, several varieties of thyroiditis (acute, subacute, and chronic), and thyroid neoplasms either benign or frank malignancies (*Lawrence and Kaplan, 2002*).

The differential diagnosis of an apparent thyroid nodule includes thyroidal and non-thyroidal conditions. Subacute thyroiditis and chronic lymphocytic thyroiditis may result in a nodular appearance; in rare cases, infiltrative disorders (e.g., hemochromatosis) or a metastatic tumor, parathyroid cyst, lipoma, or paraganglioma can mimic a thyroid nodule (*Burman and Wartofsky, 2015*).

A proper history of the present illness represents an important part of the clinical assessment. This should be targeted to search for risk factors for thyroid cancer and other useful information that would help to formulate a diagnosis and start a management strategy. Special investigations are required in suspected cases of familial disease such as familial MTC, MEN II, familial PTC, FAP, Cowden Disease, Gardner's Syndrome and Carney's Syndrome (*Galatà and Schulte, 2014*).

Thyroid function testing, including serum TSH measurement, should be performed to identify underlying

thyroid dysfunction but not to differentiate benign from malignant nodules (*Carling and Udelsman, 2014*).

Thyroid ultrasound is the first-line tool for the evaluation of patients with nodular thyroid disease. Evidence-based guidelines recommend thyroid ultrasound for all patients suspected of having thyroid nodules by either physical examination or another imaging study (*Jameson et al., 2017*).

Thyroid FNA has high sensitivity and specificity in the diagnosis of papillary thyroid carcinoma, as well as other thyroid malignancies, including medullary and anaplastic thyroid carcinoma. The sensitivity, specificity, and accuracy of thyroid FNAC are significantly improved when FNAC is performed under ultrasound guidance (*Ogilvie et al., 2012*).

The incidence of thyroid cancer continues to rise worldwide, mostly as a result of increased use of diagnostic imaging modalities and surveillance tools (*Cabanillas et al., 2016*).

Medical and/or surgical management strategies of the thyroid nodules should be guided by clinical data together with the results of ultrasound evaluation and FNAC analysis if appropriate (*Gharib et al., 2016*).

## **AIM OF THE WORK**

**T**he aim of this study is to evaluate the predictivity of different preoperative clinical findings compared to postoperative histopathological data of malignancy in patients presenting with Solitary Thyroid Nodules (STNs).