## Recent Trends in the Management of Thyroid Nodules

Essay
Submitted for Partial Fulfillment of Master Degree
In General Surgery

By

### Ahmed Al Shawadfy Abdel Aal

(M.B., B.CH.)
Faculty of Medicine - Tanta University

Under supervision of

### Prof.Dr. Mohey El Din Ragab El Banna

Professor of General Surgery
Faculty of Medicine - Ain Shams University

### Dr. Rania Mohammed El Ahmady

Assistant Professor of General Surgery
Faculty of Medicine - Ain Shams University

#### Dr. Mostafa Abdo Mohammed

Assistant Professor of General Surgery Faculty of Medicine - Ain Shams University

> Faculty of Medicine Ain Shams University 2016

## <u>Acknowledgements</u>

I would like to express my deepest gratitude and deep thanks to Prof. Dr. Mohey El Dín Ragab El Banna professor of general surgery, faculty of medicine, Ain shams university to whom I had the privilege to work under his supervision.

I would like to express my deepest thanks to Dr. Ranía Mohammed El Ahmady Assistant Professor of General Surgery, Faculty of Medicine, Ain Shams University and Dr. Mostafa Abdo Mohammed Assistant Professor of General Surgery, Faculty of Medicine, Ain Shams University for their close supervision and valuable advice. With their support, dedication and preservance, this work was produced.

Finally, I would like to express my infinite gratitude and my deepest appreciation to my family, my parents, my wife and my son Adam. None of this could have ever happened without them. And I'm forever grateful. This dissertation stands as a testament to your unconditional love and encouragement. And to all staff members and to my colleagues at general surgery department for their support.

## The index of Contents:

The Topic	Page number
Introduction	I
Aim of the work	IV
Chapter 1 Pathogenesis of thyroid nodules	1
Chapter 2 Diagnosis of thyroid nodules	23
Chapter 3 Management of Thyroid Nodules	43
Chapter 4 Treatment of Benign Thyroid Nodules	71
Chapter 5 Treatment of Malignant Thyroid Nodules	87
Summary	117
References	120
Arabic Summary	1

# List of figures

Fig.	<u>Title</u>	<b>Page</b>
<u>number</u>		<u>number</u>
Fig. 1	A colloid goiter showing a colloid	
	droplet and clusters of typical follicular	6
	cells.	
Fig. 2	Hashimoto's thyroiditis.	9
Fig. 3	Riedel's thyroiditis.	10
Fig. 4	Follicular adenoma of the thyroid.	11
Fig. 5	Hürthle cell adenoma.	12
Fig. 6	Hürthle cell adenoma.	13
Fig. 7	Hürthle cell carcinoma.	13
Fig. 8	Hürthle cell carcinoma.	14
Fig. 9	Papillary thyroid carcinoma.	16
Fig. 10	Minimally invasive follicular carcinoma	18
Fig. 11	Anaplastic carcinoma.	20
Fig. 12	Cystic thyroid nodule.	26
Fig. 13	Complex thyroid nodule.	27
Fig. 14	Radioisotope Scanning. Cold nodule.	29
Fig. 15	Radioisotope Scanning. Warm nodule.	29
Fig. 16	PET / CT.	31
Fig. 17	Nodule sonographic patterns and risk of malignancy	36
Fig. 18	Cancer risks and algorithm for clinical	
11g. 10	management of patients with cytologically	42
	indeterminate thyroid nodules.	
Fig. 19	Algorithm scheme for the diagnosis and	44
	management of palpable thyroid nodules	77
Fig. 20	Management algorithm for the	46
	evaluation of thyroid nodules.	10
Fig. 21	Thyroidectomy incision.	48
Fig. 22	MIVAT	52
Fig. 22	MIVAT	53
Fig. 24	Comparison of the RAT and RFT approaches.	54

# List of figures

Fig.	<u>Fig. number</u>	Fig.
<u>number</u>		<u>number</u>
Fig. 25	The robotic facelift thyroidectomy	55
	incision.	33
Fig. 26	Regional nomenclature of cervical	60
	lymph nodes (levels I–VII).	60
Fig 27	Percutaneous Ethanol ablation therapy.	64
Fig. 28	Axial sonographic view shows that entire	
	nodule was filled with echogenic microbubble	65
	at end of ablation.	
Fig. 29	Axial sonographic view shows trans-isthmic	65
	approach of radiofrequency electrode.	
Fig. 30	Interstitial laser photocoagulation	66
Fig. 31	Percutaneous laser ablation procedure	67
Fig. 32	Percutaneous ethanol ablation therapy	75
Fig. 33	Anaplastic thyroid carcinoma, resectable	107
	disease.	107
Fig. 34	anaplastic thyroid carcinoma, unresectable	108
_	disease	100
Fig. 35	ATC Resection bed.	110

# List of Tables

<u>Table</u>	<u>Title</u>	<b>Page</b>
<u>number</u>		<u>number</u>
Table 1	Etiology of thyroid nodules.	2
Table 2	The Bethesda System for Reporting	
	Thyroid Cytopathology:	32
	Recommended Diagnostic	32
	Categories.	
Table 3	ATA Sonographic Patterns, Estimated	
	Risk of Malignancy, and Fine-Needle	34
	Aspiration Guidance for Thyroid Nodules.	
Table 4	- 1	
1 able 4	Comparison between different	38
Table 5	Diagnostic Tools.	
Table 5	Characteristics and treatment results	70
	of radiofrequency ablation for	78
m 11 -	benign thyroid nodules.	
Table 6	Codon-directed timing of surgery	99
	by MTC-associated RET mutations.	

## List of Abbreviation

AD Anno Domino (Christian calendar concepts)
AFTN Autonomously Functioning Thyroid Nodules

AIT Autoimmune thyroiditis

AJCC American Joint Committee on Cancer

ATA American Thyroid Association ATC Anaplastic Thyroid Carcinoma

ATD Anti-Thyroid Drugs

BRAF gene responsible for synthesis of a protein called

**B-Raf** 

CEA Carcinoembryonic Antigen

CLND Central Lymph Node Dissection

CN Cranial Nerve

CNB Core Needle Biobsy

Ct Calcitonin

CT Computed Tomography

DTC Differentiated Thyroid Carcinoma EBRT External Beam Radiation Therapy

ETE Extrathyroidal Extension

<sup>18</sup>FDG-PET 18F-fluorodeoxyglucose Positron Emission

Tomography

FLUS/AUS Follicular lesion of undetermined

significance/Atypia of undetermined significance

FNA Fine Needle Aspiration

FNAC Fine Needle Aspiration Cytology

FN/SFN Follicular or oncocytic neoplasm/Suspicious for

follicular or oncocytic neoplasm

FTC Follicular Thyroid Carcinoma

Gy Gray (measure of dose of irradiation)

HCC Hürthle Cell CarcinomaH&E Hematoxylin & Eosin stainHIFU High-intensity Focused US

I Iodine

ILP Interstitial Laser Photocoagulation

### List of Abbreviation

KSTR Korean Society of Thyroid Radiology MAPK Mitogen-Activated Protein Kinase

MEN Multiple Endocrine Neoplasia

MIFC Minimally Invasive Follicular Carcinoma

MITS Minimal Invasive Thyroid Surgery
MIVAT Minimally Invasive Video-Assisted

Thyroidectomy

MNG Multi Nodular Goiter

MRI magnetic resonance imaging

MRSA Methicillin Resistant Staph Aureus MTC Medullary Thyroid Carcinoma

MWA Microwave Ablation

PDTC Poorly Differentiated Thyroid Carcinoma PEAT Percutaneous Ethanol Ablation Therapy

PET Positron Emission Tomography

PET/CT Positron Emission Tomography/ Computed

Tomography

PTC Papillary Thyroid Carcinoma

PTGs Parathyroid glands RAI Radio Active Iodine

RAT Robotic Axillary Thyroidectomy

RET Receptor Tyrosine Kinase RFA Radiofrequency Ablation

RFT Robotic Facelift Thyroidectomy

RLN Recurrent Laryngeal Nerve

SAT Subacute Thyroiditis

SMC Suspicious for malignant cells

SPECT single photon emission computed tomography

Tc Technetium
Tg Thyroglobulin

TPO-Ab thyroid peroxidase antibodies
TSH Thyroid Stimulating Hormone

TT Total Thyroidectomy

US Ultra Sound

WHO World Health Organization XRT External Beam Radiation

#### Abstract

Thyroid nodules are common and are commonly benign. The reported prevalence of nodular thyroid disease depends on the population studied and the methods used to detect nodules. Numerous studies suggest a prevalence of 2-6% with palpation, 19-35% with ultrasound, and 8-65% in autopsy data. Roughly 5% of thyroid nodules are malignant. Pathologically, thyroid nodules are classifiable into 5 types with distinct histologic features: hyperplastic, neoplastic, colloid, cystic and thyroid nodules. Diagnostic tests can determine if a thyroid nodule is benign or malignant (cancerous); this information can help to guide treatment decisions. There are several diagnostic tests; (Thyroid stimulating hormone estimation, Thyroid ultrasound, Fine needle aspiration ... etc.). The appropriate treatment for a thyroid nodule will depend upon the type of nodule. Benign nodules can usually be monitored over time. Surgery is the best treatment for thyroid nodules that are: (malignant), suspected cancerous to be cancerous noncancerous (benign) but large enough to cause problems with breathing or swallowing.

<u>Key words:</u> Thyroid, Nodules, Management, Benign, Malignant, FNAC.

#### Introduction

Thyroid surgery has had an illustrious past. Its probable beginning was with Albucasis when he recorded his experience of removal of a large goiter in 952 AD. Although there have been earlier reports of similar surgeries, their validity has not been warranted. Thereafter, it passed through a series of crests and troughs over the ages as its proponents and opponents held sway in the medical field over different periods of time. (Sarkar et al., 2015)

At one point of history, thyroid surgery was considered such a dreaded operation with a definite grim outcome that surgeons were fearful in performing it at all. However, surgeons like Theodor Billroth and his pupil Theodor Kocher ventured into this surgical domain and mastered it, thereby popularising it and allaying all fears about a dreaded outcome. Thyroid surgery has travelled a long way since then, and now, attempts are being made to perform the surgery in a way so as to make it minimally invasive. (Sarkar et al., 2015)

A thyroid nodule is a general term used to describe any mass or growth within the thyroid gland that is distinct from the surrounding thyroid tissue. A solitary nodule is a single nodule that is radiologically distinct from the surrounding thyroid parenchyma, while a multinodular thyroid is one in which there are multiple nodules that are distinct from each other and the surrounding thyroid tissue. (Erovic et al., 2013)

A dominant nodule within a multinodular goiter should be evaluated as a solitary nodule (Aimel et al., 2010).

Nonpalpable nodules detected on US or other anatomic imaging studies are termed incidentally discovered nodules or

"incidentalomas". Non-palpable nodules have the same risk of malignancy as do sonographically confirmed palpable nodules of the same size. (Haugen et al., 2016).

Thyroid nodules that produce thyroid hormone in an uncontrolled manner are referred to as autonomous nodules, "hot" nodules, or "toxic" nodules. If the nodule is filled with fluid or blood, it is called a thyroid cyst or hemorrhagic cyst. (**Erovic et al.**, **2013**)

Nodular disorders of the thyroid gland are relatively common among adults living in the USA, with an overall prevalence of about 4–7% in the general population. Most thyroid nodules are benign hyperplastic lesions, but 5–20% of thyroid nodules are true neoplasms (Goldfarb et al., 2011).

Thyroid nodules are found in about 1.5% of children and adolescents. They are more common in women, and this predisposition exists across all age groups. The prevalence of thyroid nodules within a given population depends on a variety of factors that include age, sex, diet, iodine deficiency, and therapeutic and environmental radiation exposure. (Elsabah and Mohamed, 2012)

The clinical importance of thyroid nodules rests with the need to exclude thyroid cancer, which occurs in 7–15% depending on age, sex, radiation exposure history, family history, and other factors. (**Haugen et al., 2016**)

Thyroid neoplasms are benign or malignant tumors of the thyroid gland. Benign thyroid neoplasms include follicular and Hurthle cell adenomas. Malignant thyroid nodules are classified by the types of malignant cells they contain: papillary, follicular,

medullary, or poorly differentiated (anaplastic) cells. (Erovic et al., 2013)

### AIM OF THE WORK

The aim of the essay is to spotlight the recent trends in diagnosis and treatment of thyroid nodules regarding evidence based studies, investigational trials and recent standards in management.

### Pathogenesis of thyroid nodules

#### **\*** Etiology of Thyroid Nodules and Risk for Malignancy:

The histological nature of thyroid nodules reveals in the vast majority either a cystic or solid adenoma or a colloid nodule, both of which represent various stages of nodule formation and degeneration within a nodular thyroid gland (Table 1). Indeed, 30% of nodules show a mixture of solid and cystic components, with pure thin-walled cysts being very rare. Graves' disease and chronic lymphocytic Hashimoto's thyroiditis can give rise to nodules, as may subacute de Quervain's thyroiditis or an infection. (**Procopiou and Meier, 2012**)

Less than 5% of palpable thyroid nodules are malignant. The risk of a concomitant thyroid cancer within a longstanding multinodular gland has been well investigated and is similar to that in a solitary thyroid nodule, i.e., less than 5%. (**Procopiou and Meier, 2012**)

Over 80% of the thyroid malignancies are papillary cancers, followed by follicular cancer (15%) and the rare anaplastic carcinoma (<2%) and poorly differentiated thyroid cancer (<1%), -respectively. Among the nonepithelial thyroid cancers, thyroid medullary carcinoma ranks first (<5%) with other cancers being even less frequent (thyroid lymphoma, metastatic cancers, squamous cell thyroid cancer). (**Procopiou and Meier, 2012**)