Study of serum Micro-RNA 221 Expression in Patients with Thyroid Nodules and Its Relation to Outcome

Thesis

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List of Abbreviations

Abb.	Full term
^{99}TC	*Thyroid radioactive technetium-99m scan*
ACR	*American College of Radiology ACR*
ATA	*American thyroid association*
ATC	*Anaplastic thyroid cancer*
AUS/FLUS	*Atypia of uncertain significance/follicular lesion of undetermined significance*
CEA	*Carcinoembryonic antigen*
DTC	*Differentiated thyroid cancer*
EDTA	*Ethylene diamine tetra-acetate*
FA	*Follicular adenoma*
FC	*Follicular carcinoma*
FN	*Follicular neoplasm/suspicious for follicular neoplasm*
FNA	*Fine needle aspiration*
FTC	*Follicular thyroid carcinoma*
GEC	*Gene expression classifier*
Gy	*Gray unit of absorped radiation dose*
IQR	*Inter-quartile range*
MEN	*Muliple endocrine neoplasia*
miR	*micro-Rna*
miRNA	*micro rna*
MTC	*Medullary thyroid carcinoma*
PC	*Papillary carcinoma*
PDC	*Poorly differentiated carcinoma*

List of Abbreviations (Cont…)

Abb.	Full term
PDC	*Poorly differentiated carcinoma*
PET	*Positron emission tomography*
PTC	*Papillary thyroid carcinoma*
Rad	*Unit of absorped radiation dose*
RISC	*RNA-induced silencing complex*
RLN	*Recurrent laryngeal nerve*
RT	*Reverse Transcription*
siRNA	*Short interfering RNA*
SMC	*Suspicious for malignant cells*
TBSRTC	*The Bethesda System for Reporting Thyroid Cytopathology*
Tg	*Thyroglobulin*
TIRADS	*Thyroid Imaging, Reporting and Data System*
Us	*Ultrasound*
UTR	*Untranslated region*

Abstract

A major dilemma in the diagnostic management of thyroid nodules is to determine whether it is a benign or malignant lesion and hence to determine decision for surgery. The majority of individuals with thyroid nodules are asymptomatic. The current first line of evaluation of thyroid nodules encompasses thyroid hormone laboratory tests, and ultrasonography of the thyroid gland , fine-needle aspiration (FNA) biopsy is often used to rule out cancer in thyroid nodules ,in 20–30 % of cases, however, FNAB yields indeterminate cytological results and suspicious for malignancy. Surgery was classically recommended for such indeterminate nodules for their risk of malignancy, which, overall, is about 25 % when confirmed histopathologically upon thyroidectomy. As a result, about 75 % of patients with cytologically indeterminate thyroid nodules would undergo unnecessary thyroid surgeries for nodules that prove to be benign only after surgery. Recent advances in research on thyroid carcinogenesis have yielded applications of diagnostic molecular biomarkers and profiling panels in the management of thyroid nodules. Among these markers are MicroRNAs (miRs) are small RNA sequences (19–25 nucleotides) that function to regulate the expression of genes.In this paper we aim to detect a possible of Micro-RNA 221 expression in sera of Patients With thyroid nodules and its relation to outcome after surgery.

INTRODUCTION

Thyroid nodules are extremely common and are mostly benign. Only 4%-6.5% of all thyroid nodules are cancerous ***(Lin et al., 2005).***

The majority of individuals with thyroid nodules are asymptomatic. The nodules are usually found during routine physical examination with some incidental findings seen on diagnostic imaging (e.g., ultrasound [US], computed tomography, magnetic resonance imaging, or positron emission tomography) performed for other indications ***(Mendel et al., 2004).***

Rarely, patients with thyroid nodules may complain of pain in the neck, jaw, or ear. If a nodule is large enough to compress the trachea or esophagus, it may cause difficulty with breathing , swallowing. Even less commonly, hoarseness can be caused if the nodule invades the recurrent laryngeal nerve that controls the vocal folds but this is usually related to thyroid cancer ***(Knudsen et al., 2012).***

The current first line of evaluation of thyroid nodules encompasses thyroid hormone and thyroid-stimulating hormone laboratory tests, and ultrasonography of the thyroid gland ***(Khadra et al., 2014).***

Ultrasonography is noninvasive and reveals many features relevant to the pathology of nodules. For example, an increased risk of malignancy has been associated with the presence of microcalcifications, irregular or speculated margins with no halo, marked hypoechogenicity, mostly solid composition, and taller than wider shape ***(Moon et al., 2010).***

On the other hand, presence of peripheral vascularity, round shape, isoechogenicity, spongiform appearance, smooth margins, and cystic composition are associated with benignancy ***(Moon et al., 2008).***

As such, fine-needle aspiration (FNA) biopsy is often used to rule out cancer in thyroid nodules ***(Haugen et al., 2016).***

Although FNA is a safe and widely used procedure, complications such as discomfort or local pain and self-limited small hematomas may occur. Approximately 60%- 80% of FNAs result in benign findings ***(Cibas et al., 2016).***

In 20–30 % of cases, however, FNAB yields indeterminate cytological results and suspicious for malignancy. Surgery was classically recommended for such indeterminate nodules for their risk of malignancy, which, overall, is about 25 % when confirmed histopathologically upon thyroidectomy. As a result, about 75 % of patients with cytologically indeterminate thyroid nodules would undergo unnecessary thyroid surgeries for nodules that prove to be benign only after surgery ***(Alexander et al., 2015).***

This historically represents a major dilemma in the diagnostic management of thyroid nodules, to which other conventional diagnostic modalities, such as ultrasonography, are also unable to provide definitive solution ***(Haugen et al., 2015).***

Recent advances in research on thyroid carcinogenesis have yielded applications of diagnostic molecular biomarkers and profiling panels in the management of thyroid nodules. The specific utility of these novel, clinically available molecular tests is becoming widely appreciated, especially in perioperative decision making by the surgeon regarding the need for surgery and the extent of initial resection ***(Robert et al., 2014).***

Among these markers are MicroRNAs (miRs) are small RNA sequences (19–25 nucleotides) that function to regulate the expression of genes. MiRNAs have been shown to play a key role in the regulation of gene expression and there is evidence that they are involved in a wide variety of physiological cellular processes including differentiation, proliferation, and apoptosis ***(Hatfield et al., 2005).***

AIM OF THE WORK

To detect value of Micro-RNA 221 expression in sera of Patients With thyroid nodules and its relation to outcome after surgery.