Prognostic significance of cervical lymph node metastases in differentiated thyroid cancer

Thesis submitted for partial fulfillment of M.Sc. degree in Nuclear Medicine

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Dedication:

I dedicate this research work to my parents, whom without their supplications and invocation this work would not be completed.

To my wife, who has been the wind beneath my wings.

And most of all to the Almighty Allah who gives me strength and spirit needed to complete this work.

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Abstract

Introduction: In differentiated thyroid carcinoma (DTC) lymph nodes are the most common metastatic site. **Aim :** was to evaluate if cervical lymph node (CLN) metastases significantly affect prognosis in DTC patients .

Patients and Methods:. The population of the study was composed of two groups. The first group consists of 82 patient of DTC & CLN metastasis while the second group, the control group, consists of 82 patients of DTC but without CLN metastasis. **Results:** Comparing the two groups for morbid-mortality revealed the following :

- No statistically significant differences regarding morbido-mortality in respect to age, gender, papillary pathology, tumor-size ▯ 1 cm and tumor uni-focality.
- Statistically significant differences regarding morbido-mortality in respect to follicular pathology, tumor-size ≥1 cm, tumor multi-focality, positivity of follow-up tools [Dx-WBS, TG and cervical sonography].
- The complete ablation success rate after the first dose of RAI131 was 63.4% and 81.7% in the LN and control groups respectively [*P* 0.03].
- A second ablation dose of RAI131 was needed in 36.6% vs. 18.3% in the LN and control groups respectively [*P* 0.04].
- In the LN group a third and fourth of RAI131 was given vs. none of the control group [*P* 0.001].

Key words: differentiated thyroid cancer - cervical lymph nodes - RAI-131.

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List of Abbreviations

AJCC	American Joint Committee on Cancer
ATA	guidelines American Thyroid Association guidelines
ATC	Anaplastic thyroid carcinomas
β	beta-particle
BND	Block neck dissection
BRAF	B-type Rapidly growing fibrosarcoma kinase
Ci	Curie
CLN	cervical lymph node
CLND	cervical lymph node dissection
CR	complete remission
CT	Computed tomography
DIT	diiodotyrosine
DTC	Differentiated thyroid carcinoma
DxWBS	Diagnostic 131-I whole-body scan
EANM	European Association of Nuclear Medicine
EBRT	External beam radiotherapy
ETA	European Thyroid Association
FTC	Follicular thyroid carcinoma
FDG 18 - PET	Flurodeoxy glucose 18- positron emission tomography

FNA	Fine needle aspiration
FVPTC	Follicular variant papillary thyroid carcinoma
γ	Gamma rays
GBq	Gega Bequrel
Gy	Gray
HCC	Hürthle cell carcinoma
I-123	Iodine 123
1-131	iodine 131
IRMA	immunoradiometric assay
LID	Low iodine diet
LN	lymph nodes
LT4	Levothyroxin (Eltroxin)
MBq	Mega Becquerel
mCi	milli Curie
Mev	Million electron volt
MIT	Monoiodotyrosine
MTC	Medullary thyroid cancer
MAFC	Maadi armed forces center
NIS	Sodium-iodine symporter
PTC	Papillary thyroid cancer
PTMC	Papillary Thyroid Micro carcinoma
RAI	Radioactive iodine

RIT	radioiodine therapy
RET	Rearranged transfaction
RRA	Radioiodine ablation of thyroid remnant tissue
SLN	Sentinel lymph node
SLNB	Sentinel lymph node biopsy
SND	Selective neck dissection
99m Tc	Technetium-99m
Tg	Thyroglobulin
TgAb	Anti-thyroglobulin antibodies
UK	United kingdom
TSH	Thyroid stimulating hormone
U.S	Ultrasound
USA	United states of America
WBS	Whole body scan
WDTC	Well differentiated thyroid cancer
WHO	World Health Organization

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Introduction

Thyroid carcinoma is the most common malignant endocrine tumor, which comprises 1% in all human tumors [1]. Differentiated thyroid carcinoma (DTC) (Papillary and follicular) represents approximately 80%-85% of thyroid cancer. Both have an excellent prognosis, with a 20- year survival of 90%–95% and 75%, respectively [2].

In differentiated thyroid carcinoma (DTC), lymph nodes are the most common metastatic site for which the major treatment is surgery and I-131 therapy [3] .

There is no agreement whether cervical lymph node metastases (N feature) are related to a worse prognosis in DTC patients or not [4]. It is generally accepted that cervical lymph node involvement in PTC does not affect overall survival [5] .

Despite that the role of lymph node metastases in defining prognosis (i.e. overall survival) currently remains relatively limited; the surgeon should recognize that local nodal recurrence is a significant problem for patients, associated with a high morbidity rates, usually due to invasion of the trachea or the great vessels or to recurrent laryngeal nerve involvement [6] .

Aim of the work

The aim of our study was to evaluate whether cervical lymph node (CLN) metastases are related to a worse prognosis in DTC patients or not.

We analyze patients data in terms of sex, age, pathological findings, thyroglobulin level, type of operation, pre and post ablation whole body scan, dose of ablation, response to the ablative dose, neck ultrasound, duration of follow up and lymph node metastases .

The population of the study was actually composed of two groups. The first group consists of 82 patient of DTC & CLN metastasis while the second group, the control group, consists of 82 patients of DTC but without CLN metastasis.

Chapter 1

Epidemiology of thyroid cancer

Thyroid cancer represents approximately 3% of all malignancies in the United States, with about 48,020 cases in the United States annually. These cases were predicted to result in 1740 deaths in the United States in 2011[7].Almost 75% of cases occur in women, making this the sixth most common malignancy in women. The incidence of papillary thyroid cancer has been increasing rapidly in men and women, increasing 189% in the United States between 1973 and 2003 [8] .

Pathology

Thyroid cancer (TC) has four main histological types: papillary (PTC), follicular(FTC), medullary (MTC), and anaplastic (ATC). PTC is the most prevalent type, and is three times more common in women than men [9]. There is also marked geographic, ethnic, and temporal variation in incidence rates [10].Genetic and environmental factors play a key role in modulating TC pathogenesis [11]. Papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma(FTC) are together referred to as differentiated thyroid carcinoma (DTC) [12]. Well-differentiated thyroid cancers (WDTC) represent more than 90% of thyroid cancers. Despite a number of important Clinico-pathological differences, these two subtypes are similar in their overall favorable prognosis and the ability to be stratified into low,

intermediate and high-risk groups based on a number of well established scoring systems. More than 80% of these cancers have an excellent prognosis, with a 20 year cause-specific mortality rate of <1% [13] .

Classification of Malignant Thyroid Tumors [14]

A) Primary malignant tumors

Malignant tumors of follicular cells

[Approximately 90% of thyroid tumors are derived from follicular cells]

- Papillary carcinoma
- Follicular carcinoma
- Oxyphilic or Hurthle cell carcinoma
- Poorly differentiated carcinoma.
- Undifferentiated (anaplastic) carcinoma

Malignant tumors of calcitonin-producing C cells

- Medullary carcinoma (5%)

Malignant tumors of mixed follicular and C cells

Miscellaneous epithelial tumors (rare)

- Squamous cell carcinoma.
- Adenosquamous carcinoma
- Mucin-producing carcinoma

Malignant non-epithelial tumors (rare)

- Malignant lymphoma
- Sarcomas
- Hemangioendothelioma

B) Secondary tumors

- Metastatic melanoma
- Metastatic renal cell carcinoma
- Metastatic breast carcinoma
- Metastatic pulmonary carcinoma

Differentiated thyroid carcinoma

Papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) are together referred to as DTC .

Papillary Thyroid Carcinoma

Papillary thyroid carcinoma is the most common DTC representing 75%-85%,characterized by a complex branching architecture in which the surfaces of the papillary cores are covered by neoplastic cells. The diagnostic features include nuclear enlargement and irregularity, overlapping, clearing (ground glass or Orphan Annie) appearance, which is considered the main criterion for diagnosing papillary carcinoma, nuclear grooves, and the optical phenomenon caused by cytoplasmic