

DOI: 10.36648/2254-6758.8.2.118

# Prognostic Factors and Survival of the Differentiated Thyroid Cancer: A Retrospective Study

**Hassan A Saad, Tamer Mohamed El-Shahidy\* and Mohamed Abdallah Zaitoun**

Department of General Surgery, Faculty of Medicine, Zagazig University, Egypt

**\*Corresponding author:** Tamer Mohamed El-Shahidy, Department of General Surgery, Faculty of Medicine, Zagazig University, Egypt, Tel: +201222498246; E-mail: shahidyamer@yahoo.com**Received date:** March 29, 2020; **Accepted date:** April 24, 2020; **Published date:** April 30, 2020**Citation:** Saad HA, El-Shahidy TM, Zaitoun MA (2020) Prognostic Factors and Survival of the Differentiated Thyroid Cancer: A Retrospective Study. J Univer Surg. Vol.8 No.2: 4

## Abstract

**Introduction:** The thyroid cancer incidence is increased in recent years. Thyroid cancer approximately represents 1% of all cancer diagnosed patients yearly. Prediction of the thyroid malignancies was extend from most extremely visible differentiated carcinoma; papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC), to the minimal public aggressive, however extreme aggressively growing was an anaplastic type.

**Aim of current work:** The aim of our investigation is to determine the prognostic factors, which are effecting the long-term survival in patients with differentiated thyroid carcinoma (DTC).

**Patients and methods:** The retrospective investigation was done at the surgical department, Zagazig University. Two hundred and fifty patients were influenced for DTC from 2010 to 2018. All estimated patients were categorized into 167 for PTC and 93 for FTC. Data of 250 patients have been clarified during our retrospective study. Survival data and risk factors have been concluded from follow-up documents, and from the patients reviewing.

**Results and Discussion:** Follow-up 167 patients and their survival data underwent surgery for papillary carcinoma and follow 93 for follicular carcinoma, at the surgical department, Zagazig University. The 10 years survival was 87.9% and 84.0%, respectively. Follow up time is around ten years for 2 groups. Patients of papillary carcinoma (average age: 42.7 ± 16.0 years, male: 47, female 120: (male: female ratio 1: 2.5), however in patients were operated on for follicular carcinoma (average age: 48.5 ± 14.9 years, male: 29, female: 64, male: female ratio 1: 2.2). Our findings clarified a persistent elevation in the number of patients, together with elevated papillary carcinomas proportion, and through this period of study their elevation of early average which correlated completely with our statistics.

**Conclusion:** The outcome of PTC and FTC are comparatively well with decrease tumor-related mortality,

and the survival average are get better through the past ten years because the consequence of broad prevalence recent diagnostic and curative protocols. After determining the predicted factors of survival gives us to make the suitable decision for every individualized surgical plan and the extent of the surgical intervention plane, whose needing for follow-up handling, the number or frequent follow-up care visits or outpatients clinics.

## Keywords

Prognostic factors; Thyroid; Cancer; DTC; PTC; FTC; Retrospective

## Abbreviations

PTC: Papillary Thyroid Carcinoma; FTC: Follicular Thyroid Carcinoma; DTC: Differentiated Thyroid Carcinoma

## Introduction

Thyroid cancer approximately represents 1% of all cancer diagnosed patients yearly [1]. Thyroid cancer range from almost frequently differentiated carcinoma; PTC, and FTC to less common and most aggressively nature undifferentiated anaplastic types [2,3]. The tumor specific mortality is the low mortality rate, and the life expectancy continues to be improved during the recent 10 years, due to the advanced diagnostic and therapeutic protocols tools [4]. But, several cases own bad prediction in the group, in order to of delayed ruling and unawareness and minimum learned kinds of patients [5,6].

The great variations in the handling of the thyroid malignancy are about the different planes of the surgery intervention; extend of excision indicating different protocols of postoperative treatment. The surgical operation is the fundamental handling, and lymph nodes metastases degree that simulating the patients survival rate [7,8].

Between these major principle complexities, the recurrent paralysis of the laryngeal nerve, and hypo-parathyroidism were clarified. The happening of these complexities is less popular

in the first process. It is significant to detect the volume of the surgical interference before or during process sitting [6]. The extreme revolutionary transaction, total thyroidectomy for all patients, after pre & intraoperative diagnostic methods when the result of the histology reveals carcinoma, the option will total thyroidectomy after frozen results [9].

Due to the long survival period, a good plane of surgery requires the long-range supervene. Therefore, they were claimed by retrospective studies; data from prospective studies that not yet published. The survival depends on cancer size, lymph node & remote metastases, detected by TNM classification, also other factors. The study included papillary, follicular, or both types. The long-term well prediction of differentiated thyroid carcinomas is as yet unknown causes. The immune system response is a potential demonstration of the lymphocytic infiltration which was not understood totally. The effects of iodine deficiency with above-mentioned factors have not been reported. The consequence of the ionizing irradiation on the pathogenesis of the thyroid carcinoma, is not understood good and were examined by many investigations [10,11].

## Aim of the study

The aim of our investigation is to determine the prognostic factors which are effecting the long-term survival in patients with differentiated thyroid carcinoma (DTC) as sex, age, tumor masses size, distant metastasis or not, lymph node metastasis or not, lymphocytic infiltration, degree operation effect, types of operation plan, histological characteristics of the tumor, iodine supply or deficiency, patients' TNM classification changes.

## Patients and Methods

Between 2010 and 2018, 250 patients were influenced for the differentiated types of thyroid carcinoma; 176 for papillary carcinoma and 93 for follicular carcinoma at the surgical department, ZagazigUniversity. The information's of all 250 patients have been estimated through the time of the retrospective investigation.

In 167 patients of papillary carcinoma (average age: 42.7 ± 16.0ys, male: 47, female: 120 (male: female ratio 1: 2.5), but in 93 patients were surgically processed for the follicular carcinoma (average age: 48.5 ± 14.9 years, male: 29, female: 64, male: female ratio 1: 2.2).

Survival information and complexity have been gained from the operation and post- operative documentation. The multifocality, multicentricity, iodine deficiency or supply, and lymphocytic infiltration, all were investigated in the present retrospective investigation in both PTC and FTC group, (Table 1).

**Table 1:** Prognostic risk factors Cox regression analysis (p) Papillary cc. Follicular cc.

Characteristics	Papillary cancer	Follicular cancer
-----------------	------------------	-------------------

Age of patients 40<	0.002	0.001
Tumor size	<0.0001	0.002
Metastasis	<0.0001	<0.0001
Node	<0.0001	0.170

The size of cancer, number of lymph node expanded and the remote metastases, total thyroidectomy (the complete removal of the gland) or near total (when only small suspected normal tissue about 0.5-1 cm<sup>3</sup> of either thyroid lobe is spared), close to the rear capsule to be followed by 131I ablation, to avoid recurrent laryngeal nerve injury and parathyroid removal or deprivation of blood supply (Table 2).

**Table 2:** Survival factors of PTC and FTC patients (Kaplan Meier curves - p value) of papillary cancer, Follicular cancer.

Characteristics	Papillary cancer	Follicular cancer
Gender	0.28	0.20
Age	<0.0001	0.047
Size	0.47	0.20.
T1-2-3-4	<0.0001	<0.00009
Metastasis	<0.00009	<0.0001
Node	0.009	0.046
Infiltration	0.38	0.28
Surgery	0.46	0.12
Multifocality	0.46	0.5
Encapsulation	0.04	0.07
Iodine	0.65	- 0.7

The histological samples were re-estimated again and the diagnosis was re-evaluated established on the ranking guideline were examined. The spread of lymphocytic infiltration in the tumor was series and also estimated that correlating with good prognosis. Others studies clarified that the iodine intake correlated well with the iodine level in Hungary period. The survival curve calculations were done by the SPSS in our Windows program and the data were then analyzed by Cox regression. TNM estimated changes and the surgical process types in two separate intervals of our retrospective time, also we matched happening and age distribution of the histologically and degree of differentiation of the different carcinomas types.

## Results

Following-up 167 patients and their survival data underwent surgery for papillary carcinoma and follow 93 for follicular carcinoma, at Zagazig University surgical department. 10 years survival for papillary and follicular carcinoma was 87.9% & 84.0% respectively, with average follow-up period 9.6 + for papillary type /- and 6.9 years for follicular type. In 167 patients of papillary carcinoma (average age: 42.7 ± 16.0ys,

male: 47, female 120: (female ratio 1: 2.5), but in 93 patients were surgically processed for the follicular carcinoma (average age:  $48.5 \pm 14.9$  years, male: 29, female: 64, male: female ratio 1: 2.2).

The TNM stage usually distributing between our patients. Almost of patients in stage T<sub>2</sub> (PTC: 33%, FTC: 49%). The patients gender, the age over 40 years, surgery type (total versus. near-total thyroidectomy), and lymphocytic infiltrations or multifocality that did not affect the survival rate.

Papillary carcinomas that early lymphatic metastasized to the primary neck lymph nodes. At the period of surgery, the primary, 58 (34.7%) of the 167 patients had nodal metastases, including 12 patients with stage N1b, bilateral metastases. Patients were died of the primary disease in 167 papillary patient group 2 of these patients had stage M<sub>1</sub> tumors, 3 had distant metastases (T<sub>1</sub>-3M<sub>1</sub>), and another 8 had extrathyroidal (T<sub>4</sub>M<sub>0</sub>) tumors. In the follicular group, 8 patients died of the 53. Of these, 2 had T<sub>4</sub>M<sub>1</sub> stage. Another 2 had known distant metastases (T<sub>2</sub>-3M<sub>1</sub>) at the time of surgery, and 2 patients had stage T<sub>4</sub>M<sub>0</sub>. In the follicular tumor group, all tumor concerning death happened at first decade of the following-up also.

T<sub>4</sub> tumors stage, spread of the anatomical outlines or outside the gland capsule, had importantly worst the survival than of stage T<sub>1</sub>, T<sub>2</sub>, or T<sub>3</sub> tumors, either in the PTC and FTC groups.

We can't do any procedure for stage T<sub>4</sub> patients except only palliative resection. There are no any important changes between the survival of stages for T<sub>1</sub>, T<sub>2</sub> and T<sub>3</sub> patients, only if we excluded patients of distal metastasis (Stage T<sub>4</sub> tumors) from our analysis data. Five patients with PTC and four in the FTC group had at early diagnosis of primary metastasis (died through the follow-up time) in both groups. Survivalrate changes very badly if we accompanied it with distal metastasis in all groups of patients. The incidence of lymphocytic infiltration had a perfect prognosis in both groups but not importantly influences the survival in both types.

If the metastasis of the lymph node and thyroid were present in the time of our investigation, the number of the absolute and relative frequency of PTC cases was elevated in the previous decade as opposite to the FTC between all cases. This is as the elevating the patient's number of their treated at our hospital. The ratio of early T<sub>1</sub> and T<sub>2</sub> stage between such cases that elevating gradually. Also among PTC patients, we noticed the metastasis stage of lymph node was minimized, from 40.6% to 30.8%, while minimal recurrent distant metastases in both groups.

## Discussion

The survival of DTC was influenced by multiple reasons than those detected by the generally acceptable TNM classification as tumor mass size or lymph node metastases number, site and distant metastases [10-14]. Different scoring factors and systems have been formed based on the outcome of the retrospective studies carried out before. In **Table 3**, we

compare our information's with the factors that believed main affecting factors by other authors.

**Table 3:** Prognostic factors affecting survival author type N gender size pT4.Met.Node.Multif.Infiltr. Surg. Iodine.

Author	Main affecting factors
Byar [15]	All 507 M MM
Cady [12]	DTC 755 M MM
Sanders [16]	DTC 1019 M MMn.s. n.s.
Mazzaferri [8]	DTC 1355 M MMMMMM
Sellers [17]	DTC 212 n.s. M n.s. M Mn.s. n.s.
Simpson [3]	PTC 1074 n.s. n.s. M n.s. n.s. n.s. n.s.
Hay [18]	PTC 860 n.s. M MMn.s. n.s.
Hay [19]	PTC 1779 n.s. M MMn.s. n.s. n.s. M
Akslen [2]	PTC 173 M n.s. n.s. n.s. n.s. n.s. n.s. n.s.
Kashima [20]	PTC 1533 n.s. n.s. n.s. M n.s. M
Simpson [3]	FTC 504 n.s. M MMMM
Mueller-G. [21]	FTC 149 n.s. n.s. M n.s.
Shaha [22]	FTC 228 n.s. M MMn.s.
Hay ID [23]	PTC 900 n.sn.sn.sMMn.sn.sn.s
Eustatia-Rutten CF [24]	FTC 322 n.s M n.s MMM
Hughes DT [25]	PTC 160 n.s m n.s MMMM
Kithara CM [26]	FTC 301 n.sn.sn.s M Mn.sn.sn.s
Present study	FTC 106 n.s. n.s. M Mn.s. n.s. n.s. n.s. n.s.

All- All types of Thyroid Cancer, DTC- Differentiated Thyroid Carcinoma, FTC- follicular thyroid carcinoma, Infiltr- Lymphocytic infiltration present, Iodine- iodine intake, Met- Metastasis Distant, Multif- Multifocal tumor, N- Patients' number, Node- Lymph node metastasis present, n.s.- non significant, pT<sub>4</sub>- tumor size if extrathyroidal invasion present, PTC- papillary thyroid carcinoma, Gender- patient sex, Size- size of tumor if no extrathyroidal invasion present, Surg- extent of surgery, M- significant (p < 0.05)

PTC and FTC have to be examined separated as their various biological behaviours. The patient's age examination is the extreme significant prognostic factor in both types groups, the recurrence and mortality rates which elevating after 40 years old, recurrence appears early stage, and death sooner after recurrence, indicating rapid tumor growth and mitotic rate and tumorbehaviour. Patients were surgically handled at first stages as the development and diffuse of fine-needle aspiration biopsy and US guided aspiration cytology last decades. So, with the elevating numbers of patient with papillary carcinomas, the rate of stage T<sub>4</sub> elevated. This was clarified by the comparatively elevated number of patients accepted and operates in our department. Furthermore, unluckily, it still firstly between the aged patients, those patients go to medical advice after the tumor has already keep going for nearly 10 years.

The major public process for all endocrine disease is performed for thyroid lesion as the multinodulargoiter or for a

solitary node. In the solitary thyroid nodules, it is important to keep out the chance of malignancy during the treatment, to achieve to best survival when thyroid carcinoma is operated on at an early stage.

By the assistance of fine-needle aspiration cytology guided by US has a series importance in the estimation of the predominant nodes and so the effect of the operation outline, however if the nodules were commonly 1 cm or above. For cases (C3-C5) where preoperative proven cytology or high suspected malignancy, the following operative procedures done at our hospital:

- Fine-needle aspiration cytology if -ve we proceed to the removal of the enlarged thyroid lobe or that containing the node, together with isthmus, keeping the frequent laryngeal nerve and the parathyroid glands. The lobe and the isthmus were then sent for intraoperative frozen section.
- If the quick-frozen sample indicates malignancy, we proceed to total thyroidectomy. But if the fine-needle was done only preoperative and it was conclusive we proceed to the total thyroidectomy from the start without frozen section.
- Among these patients, 7 were suffered the second operation after the first operation. Of the other 9 patients, histopathology results conclude proven residual tumor examination in 3 of the specimen removed during 7 total removal of all residual thyroid gland and 9 near-total thyroidectomies. The percent of recurrent laryngeal N. paresis is 2.4-3.6% and persistent hypoparathyroidism in 2.1 – 6.9% among the groups.

## Conclusion

The outcome of PTC and FTC are comparatively well with decrease tumor-related mortality, and the survival average are get better through the past ten yrs because the consequence of broad prevalence recent diagnostic and curative protocols. After determining the predicted factors of survival gives us to make the suitable decision for every individualized surgical plan and the extent of the surgical intervention plane, whose needing for follow-up handling, the number or frequent follow-up care visits or outpatients clinics.

## References

1. Jarzab B, Słowińska-Klencka D (2010) Comment to recommendations: Diagnostics and treatment of thyroid cancer. *Endokrynol Pol* 61: 569–574.
2. Akslen LA, Haldorsen T, Thoresen SO, Glattre E (1991) Survival and causes of death in thyroid cancer: A population-based study of 2479 cases from Norway. *Cancer Res* 51: 1234–1241.
3. Simpson WJ, McKinney SE, Carruthers JS, Gospodarowicz MK, Sutcliffe SB, et al. (1987) Papillary and follicular thyroid cancer: Prognostic factors in 1,578 patients. *Am J Med* 83: 479–488.
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, et al. (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*. 68: 394-424.
5. Wynford-Thomas D, Jones CJ, Wyllie FS (1996) The tumour suppressor gene p53 as a regulator of proliferative life-span and tumour progression. *Neurosignals* 5: 139-153.
6. Fagin JA (1995) Tumor suppressor genes in human thyroid neoplasms: p53 mutations are associated undifferentiated thyroid cancers. *J Endocrinol Invest* 18: 140–142.
7. Bilimoria KY, Bentrem DJ, Ko CY, Stewart AK, Winchester DP, et al. (2007) Extent of surgery affects survival for papillary thyroid cancer. *Annals of Surgery* 46: 375.
8. Mazzaferri EL, Jhiang SM (1994) Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *The American Journal of Medicine* 97: 418-428.
9. Belfiore A, Rosa GL, Porta GA, Giuffrida D, Milazzo G, et al. (1992) Cancer risk in patients with cold thyroid nodules: Relevance of iodine intake, sex, age, and multinodularity. *Am J Med* 93: 363-369.
10. Degroot LJ, Kaplan EL, McCormick M, Straus FH (1990) Natural history, treatment, and course of papillary thyroid carcinoma. *The Journal of Clinical Endocrinology & Metabolism* 71: 414-424.
11. Sciuto R, Romano L, Real S, Marandino F, Sperduti I, et al. (2009) Natural history and clinical outcome of differentiated thyroid carcinoma: a retrospective analysis of 1503 patients treated at a single institution. *Ann Oncol* 20: 1728–1735.
12. Cady B, Sedgwick CE, Meissner WA, Bookwalter JR, Romagosa V, et al. (1976) Changing clinical, pathologic, therapeutic, and survival patterns in differentiated thyroid carcinoma. *Ann Surg* 184: 541–553.
13. So YK, Son YI, Hong SD, Seo MY, Baek CH, et al. (2010) Subclinical lymph node metastasis in papillary thyroid microcarcinoma: A study of 551 resections. *Surgery* 148: 526–531.
14. Chow SM, Law SC, Chan JK, Au SK, Yau S, et al. (2003) Papillary microcarcinoma of the thyroid — prognostic significance of lymph node metastasis and multifocality. *Cancer* 98: 31–40.
15. Byar DP, Green SB, Dor P, Williams ED, Colon J, et al. (1979) A prognostic index for thyroid carcinoma: a study of the EORTC. *Thyroid Cancer Cooperative Group. Eur J Cancer* 15: 1033-1041.
16. Sanders LE, Cady B (1998) Differentiated thyroid cancer: reexamination of risk groups and outcome of treatment. *Arch Surg* 133: 419-425.
17. Sellers M, Beenken S, Blankenship A, Soong S, Turbat-Herrera E, et al. (1992) Prognostic significance of cervical lymph node metastases in differentiated thyroid cancer. *Am J Surg* 164: 578-581.
18. Hay ID, Grant CS, Taylor WF, McConahay WM (1987) Ipsilateral lobectomy versus bilateral lobar resection in papillary thyroid carcinoma: a retrospective analysis of surgical outcome using a novel prognostic scoring system. *Surgery* 102: 1088-1095.
19. Hay ID, Bergstrahl EJ, Goellner JR, Ebersold JR, Grant CS (1993) Predicting outcome in papillary thyroid carcinoma: development of a reliable prognostic scoring system in a cohort of 1779 patients surgically treated at one institution during 1940 through 1989. *Surgery* 114: 1050-1058.
20. Kashima K, Yokoyama S, Noguchi S, Murakami N, Yamashita H, et al. (1998) Chronic thyroiditis as a favourable prognostic factor in papillary thyroid carcinoma. *Thyroid* 8: 197-201.

21. Mueller-Gaertner HW, Brzac HT, Rehenning W (1991) Prognostic indices for tumor relapse and tumor mortality in follicular thyroid carcinoma. *Cancer* 67: 1903-1911.
22. Shaha AR, Loree TR, Shah JP (1995) Prognostic factors and risk group analysis in follicular carcinoma of the thyroid. *Surgery* 8: 1131-1138.
23. Hay ID, Gonzalez-Losada T, Reinalda MS, Honetschlager JA, Richards ML, et al. (2010) Long-term outcome in 215 children and adolescents with papillary thyroid cancer treated during 1940 through 2008. *World J Surg* 34:1192-202.
24. Eustatia-Rutten CF, Smit JW, Romijn JA, Van Der Kleij-Corssmit EP, Pereira AM, Stokkel MP, et al. (2004) Diagnostic value of serum thyroglobulin measurements in the follow-up of differentiated thyroid carcinoma, a structured meta-analysis. *Clin Endocrinol* 61: 61-74.
25. Hughes DT, Doherty GM (2011) Central neck dissection for papillary thyroid cancer. *Cancer Control* 18:83-88.
26. Kitahara CM, McCullough ML, Franceschi S, Rinaldi S, Wolk A, et al. (2016) Anthropometric Factors and Thyroid Cancer Risk by Histological Subtype: Pooled Analysis of 22 Prospective Studies. *Thyroid* 26:306-318.