

The Presentation and Management of Differentiated Carcinomas Thyroid

Management of Differentiated Thyroid Carcinomas

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ABSTRACT

Objective: Differentiated carcinomas of thyroid (DTC) are very common endocrine tumours with excellent prognosis and this study is aimed to highlight the presentation, management and outcome of the DTCs.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Surgical department of Khalifa Gul Nawaz Teaching Hospital Bannu in collaboration with the BINOR (Bannu Institute of Nuclear Medicine oncology and Radio-therapy situated in the vicinity of KGN MTI) from March 2014- March 2017 and was compiled in July 2021, after a follow up period of five years.

Materials and Methods: A total of 300 patients of DTC, including 210 (70%) female and 90 (30%) male with nodular disease of thyroid (DTC) were included in this study. Age ranged from 18-85 years with a mean age of 45 years.

Results: Out of the 300 patients with DTC, 190 were of papillary carcinoma, 90 with follicular carcinoma and 20 of mixed variety. 60 patients had lobectomy and out of these, 40 cases had completion thyroidectomy. 200 patients had total thyroidectomy and the remaining 40 cases having ipsilateral lymph nodes positive, had total thyroidectomy along with modified radical neck dissection. 130 (43%) patients had radioactive iodine therapy (in BINOR) 6-8 weeks after total thyroidectomy. 75 cases (25%) had regional and distant metastases. Altogether 7 patients died of the disease at the end of 5 years follow up. The mortality rate was 2.3%.

Conclusion: Fine needle aspiration cytology (FNAC) is a gold standard, safe, inexpensive and reliable method of confirming the diagnosis of DTC. Management of DTC requires a multidisciplinary approach consisting of thyroid specialist surgeon, pathologist and specialist in radiation oncology and nuclear medicine. Surgery is the first line treatment while radioactive iodine therapy, TSH suppression, regular physical examination and imaging investigations like ultra-sound (US), CT scan and radioactive iodine scanning of the patients, periodic thyroglobulin detection are the good strategies regarding the management of the DTC.

Key Words: Differentiated Thyroid Carcinoma (DTC), fine needle aspiration cytology (FNAC), thyroid nodule, thyroid lobectomy, total thyroidectomy, thyroglobulin (Tg), radioactive iodine (RAI), surveillance and thyroid stimulating hormone.

Citation of article: Khan GS, Amir M, Mehmood A, Gul N. The Presentation and Management of Differentiated Carcinomas Thyroid. Med Forum 2021;32(12):102-106.

INTRODUCTION

Papillary and follicular carcinomas are the differentiated thyroid cancer. DTC are the most common endocrine tumours.

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Received: September, 2021

Accepted: October, 2021

Printed: December, 2021

The incidence of these tumours has been increasing for the last few decades but the mortality remains the same¹, which is due to the increase in the number of small /occult or in situ cases diagnosis. These small cases do not contribute to mortality. Increase detection is due to improved pathological sectioning and the incidental detection of clinically occult foci on imaging performed for some other purpose^{2,3}. The survival rate of DTC is excellent so the management should have an initial oncological surgical resection, providing follow up, radioactive iodine therapy, thyroid stimulating hormone (TSH) suppression and close surveillance. Papillary carcinoma is the most common accounting to 60-80% and follicular carcinoma 10-15%⁴. Follicular carcinoma is lethal than papillary due to its vascular spread and have distant metastases. While papillary carcinoma has lymphatic spread and have locoregional recurrences. Two papers published by US and German thyroid group confirmed that the incidence of follicular carcinoma is high in the region with iodine

deficiency^{5,6}. Radioactive iodine is no longer recommended for the treatment of low risk patients with DTC. The prognosis of Papillary thyroid carcinoma (PTC) is generally good, about 10% of patients would finally die of the disease and an even a high proportion would suffer the morbidity of recurrence^{7,8}. In papillary thyroid carcinoma (PTC), there is usually a history of ionizing radiation exposure for benign or malignant disease in childhood or adult, nuclear fallout or nuclear energy accidents. DTC constitute 2% of all the body cancer⁹. Regarding the distribution of the disease, 2/3rd cases are found in women and 1/3rd in men¹⁰.

The age, sex, size of the tumour, extra thyroidal spread and completeness of resection have been found to effect the prognosis¹¹. Despite of the best practice, recurrence rate are reported from 8-23%^{12,13}. Cervical metastases occur in 35-80% cases of Differentiated papillary carcinoma¹⁴. These metastases do not adversely affect the survival rather they increase the locoregional recurrences and reoperation rate¹⁵.

Patients with recurrence disease undergo salvage surgery and radioactive iodine therapy. The mortality with recurrence has been reported as 40-50% and these patients with recurrence having an increase risk of multiple recurrences. The risk for distant metastases is 10-15% for follicular thyroid carcinoma.

MATERIALS AND METHODS

This is a retrospective study from the medical record review of 300 patients with DTC admitted to the surgical department of Khalifa Gul Nawaz Teaching Hospital Bannu, was conducted from March 2014-March 2017 and compiled in July 2021, after a follow up period of 5 years.

In this study, the record regarding the patients demography i.e. the age, sex, diagnosis and size of the tumour, solitary or multifocal, stage of the tumour, extra thyroidal spread, information about the site of recurrence (locoregional, distant or unspecified), mode of detection (clinical, FNAC, imaging, thyroglobulin estimation) and treatment (surgery/radioactive iodine¹³¹ therapy) for the primary disease and recurrence. Extent of the primary disease was retrospectively staged according to the current American Joint Committee on cancer (AJCC). Treatment success was ascertained on the basis of undetectable thyroglobulin estimation and or normalization of imaging modalities including iodine¹³¹ scanning, ultrasonography and CT scanning. Follow up was counted from completion of treatment to the last known recurrence at the end of 5 years surveillance. Outcome was written as alive with no disease, alive with disease and died of the disease. Demographic data of 300 patients treated for well differentiated thyroid carcinoma.

- Age ----- 45 (18-85) years.
- ≤45years -----190 patients.

- >45yrs -----110 patients.
- Sex F/M----- 210/90.

Histological diagnosis

- Follicular carcinoma ----- 90 cases.
- Papillary carcinoma ----- 190 cases.
- Mixed type -----20 cases.

Tumour size ----- 2.5(1-6)cm.

Multifocal -----45.

Extra thyroidal spread ----- 40.

AJCC staging;

- I -----120.
- II ----- 95.
- III -----60.
- IV -----25.

Surgery;

- Lobectomy ----- 60.
- Completion thyroidectomy ----- 40.
- Total thyroidectomy ----- 200.
- Total thyroidectomy with neck dissection -----40.

Radioactive iodine¹³¹ treatment ---130 (43%) cases.

Recurrences ----- 75 (25%) cases.

Outcome;

- Alive without disease ----- 228.
- Alive with disease ----- 65.
- Dead of the disease ----- 7.

All the patients in stage I were alive and free from the disease at the end of 5 year follow up. From stage II out of 95 patients, 70 patients were alive and free from the disease. 25 patients were alive and with recurrences. In stage III, 2 patients expired due to the disease, 20 patients were alive but with recurrences and 38 patients were alive without the disease. In stage IV there were 5 expiries and all the rest of 20 patients had multiple recurrences at the end of 5 year follow up.

STATISTICAL DATA: Cancer specific survival was calculated for each stage of the disease using Kaplan Meier's curves and the difference between the stages and or risk groups was compared by the "log rank test. The hazard risk and confidence intervals were calculated for cancer specific mortality and morbidity using Cox proportional models. The relative significance of each staging system was estimated by calculating P value. $P < 0.05$ indicates statistical significance. Statistical analysis was performed using SPSS for window 11 computer software.

RESULTS

A total of 300 patients with DTC, including male 90 (30%) & female 210 (70%), age ranging from 18-85 years with a mean age of 45 years were included in the study.

The differentiated carcinoma thyroid (DTC) included, papillary carcinoma 190 cases, follicular 90 cases and mixed type 20 cases. Out of the 190 papillary carcinoma cases, 30 cases were of micro-carcinoma

(≤ 1cm size) on histopathology of the resected specimen.

On TNM staging the number of cases were;

- Stage I ----- 120 (40%).
- Stage II ----- 95 (32%).
- Stage III ----- 60 (20%).
- Stage IV -----25 (8.3%).

The initial management;

1. Lobectomy -----60 (20%).
2. Completion thyroidectomy ----- 40.
3. Total thyroidectomy -----200 (66.7%).
4. Total thyroidectomy with ipsilateral cervical lymph node dissection----40 (13.3%).

Follow up and surveillance of the patients;

Complete follow up data were available from the patient's record. The median follow up was for 58 months (range 56-60 months). All the patients after surgery were followed with in the first 4-6 weeks to decide on the further management. The further visits were scheduled as 1 visit after every three months in the first year, every 6 months for the next 3 years and annually after that. During each visit physical examination, chest X-rays, ultra-sound or CT-scan, periodic estimation of thyroglobulin levels, having being done, seen. Distant metastasis were diagnosed on the basis of histology, radiology and radioactive iodine scanning.

Adjuvant radioactive iodine¹³¹ therapy was given to 130 (43%) patients (in BINOR) 6-8 weeks after surgery. 75 (25%) patients develop recurrences (50 female & 25 male) at the end of 5 years follow up.

Recurrences from the tumour stages were;

- Stage II ----- 10.
- Stage III ----- 40.
- Stage IV ----- 25.

Regarding the site of recurrences;

1. Regional ----- 55.
2. Distal metastasis -----15.
3. Unspecified -----5.

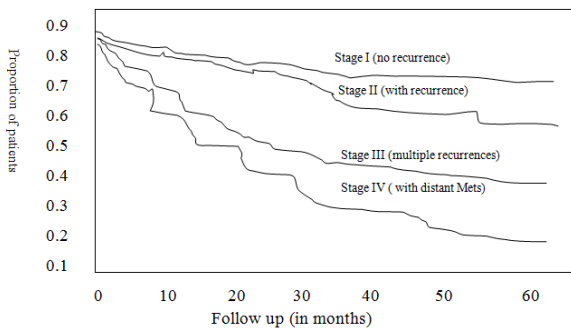


Figure No.1: Disease specific survival for patients in stages I-IV

Locoregional recurrences were seen in the cervical lymph nodes in cases of papillary carcinoma and distant metastases were seen in; clavicle, sternum, ribs, skull,

lung fields, vertebra and long bones of the limbs in cases of follicular carcinoma.

The recurrences were treated by salvage therapy including further surgery, radioactive iodine therapy and external beam radiotherapy in some cases.

Morbidity: The results of present study were quite hopeful. Initial cure was obtained in almost in 75% (225) of the cases with a recurrence rate of 25% (75) patients.

Mortality: There were 7 cancer related deaths (2 from stage III and 5 from stage IV) with a mortality rate of 2.3%. Regarding survival at the end of 5 years follow up, the stage wise figures were as follow;

- Stage I -----98.6%.
- Stage II -----98%.
- Stage III ----- 96%.
- Stage IV ----- 80%.

Hospital stay was 4-7 days with a mean of 5.5 days.

DISCUSSION

This study clears a number of important facts regarding the differentiated thyroid carcinomas. Papillary carcinoma is commoner than the follicular carcinoma in our locality. The same distribution ratio prevails in USA and UK. Our study showed that there were more deaths due to follicular carcinoma than the papillary due to its vascular spread. The median age at the initial diagnosis was 45 years and the male/female ratio 30%/70%, are comparable to that in Europe and USA. Most tumours were present in the stage I (40%) which is due to increased early diagnosis and improved pathological techniques. The same is the situation internationally.

The stage wise survival rates in our study were closely approximating the international values.

In the recent years, papillary micro-carcinoma have been increasingly diagnosed and treated in various parts of the world^{16,17}. Clinically occult tumours are mostly incidental and indolent in behavior while patients with clinically overt micro-carcinomas have a more aggressive behavior and type of presentation. Cervical metastases represent the most common focus for recurrent disease¹⁸, and that cervical mets do not affect the survival¹⁹. Cervical ultra-sound and thyroglobulin levels are commonly used for long term surveillance of PTC and are the sensitive markers for recurrent disease²⁰. Fine needle aspiration cytology (FNAC) is the gold standard for the initial evaluation of nodular disease of thyroid.

The most significant factors for the development of recurrences were male sex, advanced age and stage of the disease, the size of the tumour and the extra thyroidal spread. Male sex and age >45 years, an aggressive combination therapy consisting of surgery and radioactive iodine was used. PTC was associated with a good disease specific outcome in 60-80% of cases. In our study initial cure was obtained in most of

the patients with recurrence in only 25% cases at the end of 5 years follow up. In this study a significant better survival was observed in young female, papillary tumours and patients without distant metastases. Patients with surgery and early radioiodine therapy had a statistically significant survival versus patients with surgery and a delayed radioactive iodine therapy ($p < 0.001$). Morbidity has been reported as from 15-30% while in our study it was 25%.

In this study patients with one or more of the following risk factors were considered for radioactive iodine therapy and surgery. The risk factors were tumour size ≥ 2 cm, age >45 years, extra thyroidal spread, macroscopic post-operative residual disease in the neck and distant metastasis. For detection of mets whole body scan with iodine was performed 6-8 weeks after surgery.

Surgery was the first line treatment. Patients underwent lobectomy, completion thyroidectomy, total thyroidectomy and total thyroidectomy with lymph node dissection neck. Lobectomies were performed in some favorable cases e.g. young age, micro papillary carcinoma and minimally invasive follicular carcinoma with indolent histologies. Some cases of Lobectomies were converted to completion thyroidectomy on the basis e.g. multi-focality on the histology of resected specimen, unfavorable histology, old age and male sex. Total thyroidectomy was performed on large tumour (size >2 cm) and multi-nodular thyroid disease. While total thyroidectomy with cervical lymph nodes dissection was performed in cases of positive cervical lymph nodes. Routine palpation and sampling/clearance of the lymph nodes in the central compartments neck (group VI cervical lymph nodes) was done in cases of total thyroidectomy.

Early detection of the disease by estimation of thyroglobulin and iodine scanning are prognostically good as the disease is picked up in the early stages. Unspecified recurrences were those cases of total thyroidectomies where the Tg levels were high but on imaging or scanning no mets were detectable.

The cases of recurrences were subjected to salvage surgery, radioactive iodine and external beam radiotherapy in a few cases.

CONCLUSION

There is a progressively an increasing trend in the DTC incidence. Follicular carcinoma is lethal than papillary carcinoma due to its vascular spread. A multidisciplinary approach is needed in the management of DTC. Surgery is the first line treatment modality. Presently there is an increase in the detection of early stage DTCs. whatever is the size, stage, sex and grade of the DTC, prognosis is a good in young patients i.e. between 21 and 45 years. Management of DTC includes surgery, radioactive iodine therapy, TSH suppression and periodic estimation of thyroglobulin level.

Author's Contribution:

Concept & Design of Study: Gul Sher Khan
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 Revisiting Critically: Gul Sher Khan,
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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