

Original Article

Central Compartment Involvement in T3 & T4 Papillary Thyroid Carcinoma

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Abstract:

Background: *Lymphatic metastasis in papillary thyroid cancer (PTC) is common; however, the extent of central compartment lymph nodes dissection (CCD) is controversial and requires the knowledge of pattern for central compartment (level VI) lymph nodes metastasis (CCM).*

Objective: *To determine the frequency of central compartment (level VI) lymph node metastasis in T3 & T4 papillary thyroid carcinoma.*

Methods: *This study was conducted in the Department of Otolaryngology-Head & Neck Surgery, BSMMU, Dhaka, from January 2019 to June 2020. A total of 31 cases of T3 & T4 PTC were selected after obtaining clearance and approval from the IRB of BSMMU; the subjects were included based on the inclusion and exclusion criteria. After taking informed written consent detailed history and examination was done. Ultrasound neck and fine-needle aspiration cytology was taken from all thyroid swelling. All patients had underwent total thyroidectomy with central compartment dissection. The data were analyzed by computer-based statistical software SPSS version 26. Results were expressed as frequency and percentage. Z proportion test was done as applicable.*

Results: *In this study, mean (\pm SD) tumor size was 3.66 (\pm 1.34) cm. 20 (64.52%) had T3 and 11 (35.48%) T4 PTC. 11 (35.48%) had N0, 20 (64.52%) N1a and 8 (25.81%) N1b. 20 (64.52%) had overall central compartment lymph nodes metastasis. Among T3 papillary thyroid*

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carcinoma, 12 (60%) had overall central compartment lymph nodes metastasis, and in T4 papillary thyroid carcinoma, 8 (72.7%) had overall central compartment lymph nodes metastasis. This difference was not statistically significant.

Conclusion: The frequency of central compartment (level VI) lymph node metastasis (CCM) is high (64.52%) in T3 & T4 papillary thyroid carcinoma. So central compartment (level VI) should be dissected in advanced (T3 & T4) papillary thyroid carcinoma.

Key words: Papillary carcinoma thyroid, Central compartment lymph nodes metastasis.

Introduction:

Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer¹, representing 65 percent to 85 percent of all thyroid cancer cases². It occurs more frequently in women and presents within the 20–55-year age group. It is also the predominant cancer type in children with thyroid cancer and in patients with thyroid cancer who have had previous radiation to the head and neck³. It is well-differentiated, slow-growing, and localized, although it can metastasize.

Exposure to radiation is a proven risk factor in the aetiology of papillary thyroid cancer⁴. The thyroid gland is likely to be exposed to radiation more than other tissues because of its position in the body and its ability to concentrate iodine. Other known risk factors for thyroid cancer are non-modifiable with patient age, sex, ethnicity, and family history serving as the strongest predictors of risk¹. Women have approximately 3–4 times higher incidence of thyroid cancer than men, this ratio has remained constant over time and across countries⁵. This difference is more pronounced for PTC compared to other histological subtypes⁵.

PTC has the predilection for lymphatic spread⁶. Like any other head and neck malignancy, the lymphatic spread of PTC is supposed to follow a sequential pattern with the central compartment (level VI) lymph nodes being first to involve⁷, which besides containing the pre and para tracheal lymph

nodes, also contains the parathyroid glands and recurrent laryngeal nerves on either side, which are prone to injury while dissecting the central compartment lymph nodes⁷.

A high incidence of occult metastases of central LNs in patients with clinically node-negative PTC has been reported at up to 61%⁸.

The 2009 ATA consensus statement on the relevant anatomy and terminology the lymph nodes of the central neck compartment are divided into discrete subcompartments, based on anatomic location, which may be independently dissected during CND for PTC. These discrete nodal packets are the prelaryngeal lymph nodes; pretracheal lymph nodes; right paratracheal lymph nodes; and left paratracheal lymph nodes. Level VI lymph node boundaries are defined superiorly by the hyoid bone, inferiorly by the sternal notch, laterally by the medial aspect of the carotid sheath, posteriorly by the prevertebral fascia, and anteriorly by the superficial layer of the deep cervical fascia⁹.

The central compartment lymph nodes dissection (CCD) in PTC has the benefits of complete clearance of the disease, thereby reducing the chances of recurrence and also the subsequent morbidity of reoperation; it also provides the precise nodal staging to plan further adjuvant therapy and prognosticate the patient^{10,11}. However, it is associated with an increased risk of hypoparathyroidism and recurrent laryngeal nerve palsy¹². Therefore, for high-risk with clinically involved nodes the

routine CCD is acceptable; however, It is controversial for low-risk, clinically uninvolved nodes¹³, some advocating for^{14,15} and some against⁸ routine bilateral clearance while the 3rd group of surgeons adopted a midway, thus sparing the contralateral parathyroid glands and recurrent laryngeal nerve, by dissecting the ipsilateral side only^{16,17,2}.

However less published data are available in our country. Therefore, this present study has been designed to assess the frequency of central compartment lymph node metastasis in T3 & T4 papillary thyroid carcinoma.

Study Procedure:

Patients admitted at the Department of Otolaryngology-Head & Neck Surgery at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, with T3 & T4 papillary thyroid carcinoma. The patients were selected based on the inclusion (Clinically and/or sonographically and/or cytologically proven T3 & T4 Papillary thyroid carcinoma) and exclusion (papillary thyroid carcinoma other than T3 & T4, patients with other pathologic types of thyroid disease, re-operative surgeries (like completion thyroidectomy and loco-regional recurrence), patients who were not willing to participate in the study) criteria. After taking informed written consent from the patients, detailed history (dysphagia or change of voice to evaluate advance disease) and clinical examination (hard & fixed swelling to evaluate advance disease), ultrasound neck and fine-needle aspiration cytology of the thyroid nodules and any suspicious cervical lymph nodes, CT scan of the neck & chest in selective cases (extra-thyroidal extension, tumour involving carotid vessels & sternocleidomastoid muscle, pulmonary metastasis, pre-vertebral soft tissue, retro-sternal extension and massive lymphadenopathy) were done, after that a

preoperative clinical staging were done based on 8th AJCC. The final staging was done after the histopathology report (p-TNM). We did thyroidectomy with the standard technique of capsular dissection. The thyroid, along with the central compartment (level VI) lymph nodes, was removed enbloc (removal of the pretracheal, prelaryngeal, and bilateral paratracheal lymph node bearing tissue) in all the cases, and the fibrofatty tissue was divided in the midline and sampled. Formal lateral lymph nodes dissection involving the level II, III, and IV were done in patients with proven lateral lymph nodes metastasis. We have routinely identified all the parathyroid glands, the external branch of superior laryngeal nerves, and recurrent laryngeal nerves and save them in situ. Any at-risk parathyroid glands were auto transplanted in the sternocleidomastoid muscle. We were gross the specimen in the operation theatre and pathology department. Along with detailed grossing of the thyroid, the individual lymph nodes from lymph nodes basins were also separate, count, and embedded. Following processing, 3µm thick sections were examined under a microscope. All the slides were conducted and reported in the same institution (BSMMU). Statistical data were entered in the statistical package for social science (SPSS-26) to analyze all quantitative analysis (mean and standard deviation) and qualitative variables (frequency and percentages).

Results:

In this study, the majority 25 (80.65%) were in the age group of <55 years, and only 6 (19.35%) were in the age group of ≥55 years, respectively. The youngest and the oldest patients were 11 and 59 years, respectively. Among the study subjects, the majority 19 (61.29%) of the subjects were female. Only

12 (38.71%) were male. Male female ratio was 1:1.5.

In this study, the majority (27) of study subjects were presented with solitary nodules (87.1%), and only 4 (12.9%) presented with multinodular goiter. Only 3 (9.68%) study subjects presented with occult papillary thyroid carcinoma. In this study, the majority (26) of study subjects were euthyroid (83.87%), and only 5 (16.13%) cases were found as hypothyroid.

Among the study subject, the majority (20) of the study subjects had T3 papillary thyroid carcinoma (64.52%), and 11 (35.48%) had T4 papillary thyroid carcinoma. Most of the cases (83.87%) were node-negative, and only 5 (16.13%) cases were node-positive on clinical examination (Table-I).

Table-I :

Distribution of patients according to clinical TNM classification (N=31)

| TNM classification | Study subjects |
|----------------------|----------------|
| Tumor staging | |
| T3 | 20 (64.52%) |
| T4 | 11 (35.48%) |
| Nodal staging | |
| N0 | 26 (83.87%) |
| N1 | 5 (16.13%) |

In this study, total thyroidectomy (TT) with central compartment dissection (CCD) was done in all cases (100%). Only 8 (25.81%) patients also underwent unilateral modified radical neck dissection (Figure-1).

In this study, tumor size was <4 cm in 16 (51.61%) cases and > 4 cm in 15 (48.39%) cases. Mean (±SD) tumor size was 3.66 (±1.34) cm. Majority 20 (64.52%) had T3 and 11 (35.48%) T4 papillary thyroid carcinoma. Among T3 papillary thyroid carcinoma 5

(16.13%) had T3a (intrathyroidal) and 15 (48.39%) T3b (extrathyroidal extension). 10 (32.26%) had multicentricity, 8 (25.81%) bilaterality and 26 (83.87%) extrathyroidal extension. Among the nodal metastasis, 11 (35.48%) had N0, 20 (64.52%) N1a and 8 (25.81%) N1b. 20 (64.52%) had overall central compartment lymph nodes metastasis (Table-II).

Among T3 papillary thyroid carcinoma (n=20),

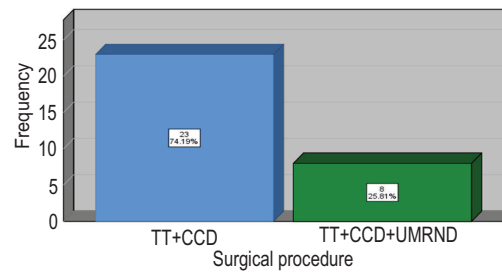


Fig.-1: Distribution of study subjects according to the methods of surgery (N=31)

12 (60%) had central compartment lymph nodes metastasis. Among 20 T3, 3 (15%) had T3a, and 9 (45%) had T3b. In T4 papillary thyroid carcinoma (n=11), 8 (72.7%) had overall central compartment lymph nodes metastasis (Table-III). Among the study subject, only 4 (12.90%) cases developed temporary hypocalcaemia, and 1 (3.23%) case recurrent laryngeal nerve palsy, and 2 (6.45%) cases hypoparathyroidism (Figure-2).

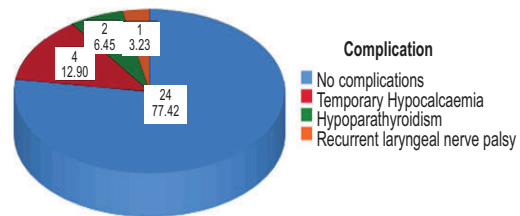


Fig.-2: Distribution of study subjects according to postoperative complications (N=31)

Table II :
Distribution of patients according to clinicopathological findings (N=31)

| Variable | Study subjects (N=31) |
|--|--------------------------|
| Tumor size (cm) | |
| <4 | 16 (51.61%) |
| > 4 | 15 (48.39%) |
| Tumor staging | |
| T3 | 20 (64.52%) |
| T3a (intrathyroidal) | 5 (16.13%) |
| T3b (extrathyroidal) | 15 (48.39%) |
| T4 | 11 (35.48%) |
| Multicentricity | 10 (32.26%) |
| Bilaterality | 8 (25.81%) |
| Extrathyroidal extension | 26 (83.87%) |
| Nodal metastasis | |
| N0 | 11 (35.48%) |
| N1a | 20 (64.52%) |
| N1b | 8 (25.81%) |
| Overall central compartment lymph nodes metastasis | 20 (64.52%) |

Table III :
Association of nodal metastasis with T3 and T4 papillary thyroid carcinoma (N=31)

| Variable | Overall central compartment lymph nodes metastasis | p value T3 vs T4 |
|------------|--|---------------------|
| T3 (n=20) | 12 (60%) | |
| T3a (n=5) | 3 (15%) | 0.478 ^{ns} |
| T3b (n=15) | 9 (45%) | |
| T4 (n=11) | 8 (72.7%) | |

Discussion:

The present study was undertaken to find out the central compartment (level VI) lymph node

metastasis in T3 & T4 papillary thyroid carcinoma. For this study, a total number of 31 cases of papillary thyroid carcinoma that meet the inclusion criteria were selected. All the data were compiled and appropriately sorted and analyzed statistically using the Statistical Package for Social Science (SPSS-26). The level of significance was calculated at $p < 0.05$.

PTC has a propensity for lymphatic spread. The metastasis is found in 20–50% of lymph nodes examined by conventional pathologic examination, whereas the rate of micrometastasis is much higher in clinically node negative-cases. The lymph node metastasis in papillary thyroid cancer has been found to have a significant impact on disease-free and overall survival of patients.

The results of the current study demonstrate that papillary thyroid carcinoma was more frequently occurs in the younger population than older. The youngest and the oldest patients were 11 and 59 years, respectively. Almost similar findings were observed by various researchers from different countries^{18,19}. But Sari et al., (2010) disagreed with our study. They reported a relatively older population was affected more²⁰.

In the present study, the majority were female. Almost similar findings were observed by various researchers from different countries^{20,18,21}. American Thyroid Association (2014) reported that women are more likely than men to have thyroid disease. One in eight women will develop thyroid problems during her lifetime.

In the present study, most study subjects were presented with solitary nodules, only a few patients presented with multinodular goiter and **occult papillary thyroid carcinoma**. Almost similar findings were observed by Agarwal et al., (2012)¹⁸ and Song et al., (2016)²². But Ali and Abde

Hameed(2018) disagreed with our study. They found multinodular goiter in their study²¹.

In the present study, all the study subjects were T3 and T4 papillary thyroid carcinoma. Most of the study subjects were node-negative on clinical examination. The majority of study subjects were euthyroid, and only a few cases were found as hypothyroid. Almost similar findings were observed by various researchers from different countries^{18,19}.

In the present study, total thyroidectomy (TT) with central compartment dissection (CCD) was done in all cases. Only a few patients needed to undergo unilateral modified radical neck dissection. Goyal et al., (2017) observed similar findings²³. But Song et al., (2016) performed thyroidectomy and lobectomy only²². These differences may be due to variations in their methods.

According to clinicopathological findings, the mean (\pm SD) tumor size was 3.66 (\pm 1.34) cm. All the subjects were suffered from T3 or T4 papillary thyroid carcinoma with N0, N1a, and N1b nodal metastasis. Carcinoma had multicentricity, bilaterality, intrathyroidal and extrathyroidal extension. The majority had overall central compartment lymph nodes metastasis (CCM). Agarwal et al., (2012), Song et al., (2016), and Ali and Abdel Hameed (2018) agreed with our findings^{18,22,21}.

Among all T4 papillary thyroid carcinoma patients (11), the histological report showed 8 (72.7%) had overall central compartment lymph nodes metastasis and 12 (60%) had overall central compartment lymph nodes metastasis in T3 papillary thyroid carcinoma (20). Almost similar findings were observed by various researchers from different countries^{18,19,22}.

In this series at the time of operation, we routinely identified all the parathyroid glands, the external branch of superior laryngeal nerves, and recurrent laryngeal nerves and

tried to save them in situ. Any at-risk parathyroid gland was autotransplanted in the sternocleidomastoid muscle. During operation, strict asepsis was followed in every step, and broad-spectrum intravenous antibiotic was given for three days. Initial recovery was uneventful in the cases. Only four subjects developed temporary hypocalcaemia, two subjects developed hypoparathyroidism, and one subject developed recurrent laryngeal nerve palsy. This finding was an agreement with the study of many researchers from different countries^{18,19,22}.

Conclusion:

The results show that the frequency of central compartment lymph node metastasis (CCM) is high (64.52%) in T3 & T4 papillary thyroid carcinoma. Multicentricity, bilaterality, extrathyroidal extension and tumour size are an important risk factor for CCM. So, central compartment (level VI) should be dissected in advanced (T3 & T4) papillary thyroid carcinoma.

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