Bull Cancer 2016; □□: □□□

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Original article

Evaluating the influence of prophylactic central neck dissection on TNM staging and the recurrence risk stratification of cN_0 differentiated thyroid carcinoma

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Received 17 October 2015
Accepted 14 April 2016
Available online:

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Évaluation de l'impact du curage cervical central prophylactique sur la stadification TNM et sur l'évaluation du risque de récidive des carcinomes thyroïdiens différenciés cN0

Keywords
Prophylactic central neck dissection (pCND)
Differentiated thyroid carcinoma (DTC)
TNM staging
Recurrence risk stratification (RRS)
Risk factors
Central lymph node metastasis (CLNM)

Summary

Objective > The purpose of this study was to explore the risk factors that were associated with central lymph node metastasis (CLNM) in patients with clinical nodal negative differentiated thyroid carcinoma (cN_0 DTC) after prophylactic central neck dissection (pCND). The influence of pCND on TNM staging and recurrence risk stratification (RRS) in patients with cN_0 DTC was also evaluated in our study.

Methods > A total of 153 cN_0 DTC patients in Guangdong general hospital who underwent thyroidectomy with pCND from March 2014 to October 2014 were enrolled in this study. The relations of CLNM with clinicopathologic characteristics of cN_0 DTC were analyzed by univariate and multivariate logistic regression. The influence of pCND on migration of TNM staging and RRS in cN_0 DTC was observed.

Results > In the present study, CLNM was found in 42.5% (65 of 153 cases) of patients with cN_0 DTC. On univariate analysis, the age less than 45 years old, tumor size more than 2 cm, pT staging, and a total number of central lymph nodes dissected more than 3 were significantly associated with CLNM ($P < 0.05$); however, gender, tumors affecting both lobes, multifocality, capsular invasion, and Hashimoto's thyroiditis were not related with CLNM ($P > 0.05$). On multivariate logistic regression, age < 45 years ($P = 0.001$) and a total number of central lymph nodes

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To cite this article: Lin X, et al. Evaluating the influence of prophylactic central neck dissection on TNM staging and the recurrence risk stratification of cN_0 differentiated thyroid carcinoma. Bull Cancer (2016), http://dx.doi.org/10.1016/j.bulcan.2016.04.003

dissected > 3 (P = 0.002) were significantly associated with CLNM. Because of the identification of CLNM in the implementation of pCND, 15 (9.8%) of 153 cN_0 DTC patients were upgraded in TNM staging; all these patients were older than 45 years. Fifty-six patients (36.6%) developed higher RRS (from low to intermediate) after pCND.

Conclusions > For younger patients (age < 45 years), careful preoperative assessment of the lymph node status must be done; surgeons should consider this risk factor when deciding whether to perform pCND. Thorough lymphadenectomy in the implementation of pCND can avoid residual lymph node metastasis and help to increase the incidence of CLNM. pCND can indentify occult CLNM which allows more precise TNM staging (for patients with age $\geq$ 45 years) and RRS.

Introduction

Thyroid cancer is the most common endocrine malignancy. Its incidence has increased dramatically in the last few decades (almost 310% between 1950 and 2004) [1]. There are three main histological types of thyroid cancer: differentiated (including papillary, follicular and Hürthle), medullary, and anaplastic cancer. Differentiated thyroid cancer (DTC) is the most common type of thyroid cancer, accounting for about 94% of all cases [2]. Studies have reported that lymph node metastases are associated with increased rates of recurrence and worse overall survival of patients with thyroid cancer [3–5]. The central compartment is the most common site of lymph node metastases. Preoperative ultrasound investigation of central compartment is technically difficult and often unreliable. Thirty-three to fifty-four percent of cN_0 DTC patients were identified with central lymph node metastasis (CLNM) after prophylactic central neck dissection (pCND) [6,7]. There is consensus that therapeutic central neck dissection should be performed in the presence of clinical lymph node metastases in central compartment [8]. However, it remains controversial regarding pCND in patients with no evidence of clinical lymph node involvement. Concerns about pCND revolve around whether its potential higher incidence of complications can be outweighed by improved local recurrence control and survival benefit [9–13]. Therefore, the aim of the current study was to explore the risk factors that were associated with CLNM and assist surgeons in determining whether to perform selective pCND in patients with cN_0 DTC. Moreover, TNM staging and recurrence risk stratification (RRS) have important prognostic values for thyroid cancer. We hypothesized that CLNM that were identified in the implementation of pCND would lead to migration of TNM staging and RRS. The influence of pCND on TNM staging and RRS in patients with cN_0 DTC was also evaluated in our study.

Materials and methods

A total of 153 cN_0 DTC patients in Guangdong general hospital who underwent thyroidectomy with pCND from March 2014 to October 2014 were enrolled in this study. Preoperative assessment included ultrasonography, computed tomography (CT) scan, fluoro-18-deoxyglucose positron emission tomography (PET), chest X-ray, and measurement of thyroglobulin (Tg), thyroid stimulating hormone (TSH) and anti-Tg antibody levels. Ultrasonography was performed preoperatively to assess the lymph node status and confirm no lymph node involvement in all these patients. CT scan and PET were used to determine the extent of tumor invasion or exclude distant metastases in some patients as needed.

The following information were collected from the medical records of the patients: gender, age, tumor size, ultrasonographic findings, diseased lobe, multifocality, capsular invasion, presence of Hashimoto's thyroiditis, total number of central lymph nodes dissected, TNM staging, RRS, and postoperative complications. There were 108 women and 45 men, ranging in age from 17 to 82 years, with a mean age of 43.1 $\pm$ 13.1 years. Patients with tumor diameter > 2 cm on ultrasonography were in 33 cases, with tumor diameter $\leq$ 2 cm in 120 cases. Single lobe diseases were found in 115 patients, both lobe diseases in 38 patients. Pathologic observation revealed 37 tumors with capsular invasion and 26 tumors with Hashimoto's thyroiditis. Multifocal tumors were found in 49 patients, compared with unifocal tumor in 104 patients. Number of dissected lymph nodes > 3 was in 58 cases, with number of dissected lymph nodes $\leq$ 3 in 95 cases. All patients were staged using the American Joint Committee on Cancer (AJCC) criteria. RRS was according to the risk stratification of the American Thyroid Association. The association between CLNM and clinicpathologic features of cN_0 DTC was analyzed in this study.

According to the revised American Thyroid Association (ATA) guidelines, total or near-total thyroidectomy is the standard surgical treatment for PTC with tumors > 1 cm in size unless there are contraindications [8]. Thyroid lobectomy is suggested for small < 1.0 cm, low-risk, unifocal, intrathyroidal papillary carcinomas in the absence of cervical lymph node metastasis [8,14]. Among the 153 patients in our study, total/near-total thyroidectomy plus bilateral pCND was performed in 141 patients, and thyroid lobectomy plus ipsilateral pCND was carried out in 12 patients. These 12 patients were confirmed by pathologic observation to have low-risk thyroid microcarcinoma without CLNM. If pathologic results of frozen paraffin