Background

Papillary thyroid carcinoma (PTC) spreads preferentially through lymphatic system to the neck lymph nodes and almost 40% of patients could have occult lymphatic metastases. Such metastases could impact in survival of these patients. Appropriate staging of these patients is still lacking. Radical central compartment dissection in these patients is still controversial as a standard due to the inherent risks of hypocalcemia and recurrent laryngeal nerve injury. Sentinel lymph node biopsy (SLNB) has become a revolutionary concept in staging many cancers, such as malignant melanoma, breast cancer and has also been suggested in oral/oropharyngeal, penis and vulvar cancers. The aim of this study was to evaluate the performance of SLNB in detecting occult metastases in PTC and to correlate it to histology of the primary tumor and patient characteristics.

Methods

Twenty-three clinically node negative PTC patients (21 females, mean age 48.4 years were prospectively enrolled. Ultrasound guided peritumoral injections of 99mTc-phytate (7.4 MBq) were performed. Patients were submitted to SLN lymphoscintigraphy prior to total thyroidectomy. SPECT/CT neck images were acquired 15 minutes after radiotracer injection and 2 hours prior to surgery. Intra-operatively, sentinel lymph nodes (SLN) were located with a gamma probe and removed along with non-SLNs located in the same neck compartment. PTC, SLNs and non-SLNs were submitted to histopathology analysis.

Results

SLNs were located in levels: II in 34.7% of patients; III in 26%; IV in 30.4%; V in 4.3%; VI in 82.6% and VII in 4.3%. Metastases in the SLN were noted in 7 patients (30.4%) and in non-SLN in 3 patients (13.1%). Metastases in the lateral compartments occurred in 20% of patients. There were significant associations between LN metastases and the presence of angio-lymphatic invasion (p = 0.04), extra-thyroid extension (p = 0.03) and tumor size (p = 0.003). No correlations were noted among LN metastases and patient age, gender, stimulated thyroglobulin levels, positive surgical margins, aggressive histology and multifocal lesions.

Conclusion

SLNB could be a staging procedure for PTC, specially for large tumors. It may help guide future neck dissection, patient surveillance and radioiodine therapy doses.

Keywords: Sentinel lymph node. Papillary thyroid carcinoma. Differentiated thyroid cancer. SPECT/CT. Sentinel lymph node biopsy. Lymphoscintigraphy.
Background

Patients with >5 positive lymph nodes (Sugitani 2004) or nodes over 1.5 cm in size (Ito 2007) are generally considered to be at high risk for nodal recurrence. The aim of our study was to determine central compartment lymph node (LN) characteristics predictive of outcomes in patients with positive central LNs.

Methods

An institutional database of 3664 previously untreated patients with DTC operated between 1985 and 2010 was reviewed. Five hundred and ninety-nine pN1aM0 patients on histopathology were identified. These patients comprised patients having a central neck dissection for macroscopic lymph nodes on clinical or radiologic examination. We also included patients with occult metastases found in perithyroidal lymph nodes, node sampling or following central neck dissection for T3 primary tumors. Patient demographics, number of positive LNs, size of largest LN, and presence of extracapsular extension (ECS) were recorded for each patient. Receiver operator curves were used to identify the significant cutoff points for number of positive nodes and size of largest lymph node. Variables predictive of neck recurrence free survival (NRFS) were identified using the Kaplan-Meier method.

Results

The median age of the cohort was 41 years (range 12-91). The median follow up was 61 months (range 1-330). Neck recurrence occurred in 43 patients. Recurrence occurred in central neck in 11 patients, the lateral neck in 27 patients and both compartments in 5 patients. LN characteristics predictive for neck RFS on univariate analysis were >8 positive LNs (5 yr NRFS 75.7% vs 91.8%, p=0.001), LN diameter greater than 7.5mm (5 yr NRFS 83.7% vs 94.9%, p=0.007), and presence of ECS (5yr NRFS 84.7% vs 94.5%, p=0.001). Gender, age, histology, and postoperative radioactive iodine administration were not predictive of NRFS on univariate analysis. Multivariate analysis controlling for T stage showed that ECS was a significant predictor for neck recurrence (HR 2.90, 95%CI 1.39-6.05, p=0.004). No LN features were predictive of distant RFS or disease specific survival (DSS) on univariate analysis.

Conclusion

The presence of ECS in positive central neck LNs is an independent predictor of neck recurrence. No LN characteristic is predictive for distant RFS or DSS.
Impact of Elective Central Compartment Lymph Node Dissection in Differentiated Thyroid Cancer on Survival

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Background and Purpose: The battle of thyroid cancer is thought to be lost in the central compartment. The present study assesses whether elective central compartment lymph node dissection (CLND) impacts cause specific survival in differentiated thyroid cancer.

Methods: 2114 consecutive patients with differentiated thyroid cancer were identified from a population based thyroid cancer cohort (1970-2010) with a median follow-up of 12 years. Outcome of these patients in terms of overall, disease specific (DSS) and disease free survival (DFS) was calculated by Kaplan Meir method and inter-group comparisons were made by log rank test. Cox proportional hazard model and competing risk sub-hazard were used for multivariate analysis.

Results: Mean age at diagnosis was 47.3 + 17.1 years. 76.7% of the patients were female, 83.2% had papillary carcinoma and 67.8% had stage I disease. 25.1% of the patients were node positive and 32.5% had CLND. 4.2% patient failed in central compartment of neck and 2.8% in lateral compartment of neck. 7.7% in those who had central compartment lymph node dissection failed in central compartment versus 2.7% who did not have central compartment clearance (p<0.001). In 56.1% of the central compartment neck failures were post central compartment lymph node dissection however there was no significant survival difference between those who had CLND and those who did not have it. There was no difference in the cause specific survival of the two groups (p=0.342). On multivariate analysis age at diagnosis, gender, T3/T4 tumor stage, metastatic disease and completeness of resection were the only factors which had significant influence on DSS.

Conclusions: Elective CLND did not provide any significant survival advantage over wait and watch policy in well differentiated thyroid cancer.
S118  CERVICAL LYMPH NODE METASTASES IN PAPILLARY THYROID MICROCARCINOMA. ¿IS IT AN UNFREQUENT EVENT?

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Introduction: Due to the low frequency of cervical lymph node metastasis (LNM) in papillary thyroid microcarcinoma (PTM), its surgical management is still under debate. The aim of this study was to quantify the frequency and risk factors of lymph node metastases in PTM with systematic biopsy of central and lateral compartment.

Methods: A retrospective study was conducted in 600 patients with differentiated thyroid carcinoma who underwent a total thyroidectomy. Lymph node biopsy of both central and lateral compartments was undertaken in all of the patients and therapeutic neck dissection was performed only when lymph node metastasis was confirmed.

Results: Out of the 600 patients, 292 (48.6%) where diagnosed as PTM (tumor size no larger than 10 mm). The median age of patients was 45 y/o. Females (n=249) and males (n=43) were enrolled in the study. Multicentric disease was present in 17 % and extracapsular invasion in 23 % of the cases. LNM were found in 37 (12.6%) patients 8 (22%) had palpable cervical nodes and the remaining 29 (78%) had clinically unremarkable examination. Of the 37 cases mentioned previously, 19 (51%) had central compartment involvement, 9 (24%) presented both lateral and central compartment involvement, and the remaining 9 (24%) had lateral compartment involvement without central node metastasis (skip metastases). Multivariate analysis showed that younger age (p = 0.001), palpable adenopathy (p = 0.0001), multicentricity (p = 0.005) and extracapsular invasion (p = 0.0001) were independent risk factors of having LNM.

Conclusions: Even though patients with PTM have a favorable outcome, they have the same risk factors of developing LNM than larger tumors. Surgical exploration methods such as routine lymph node biopsy have proved to be useful in early detection.
LONG-TERM RESULTS OF OBSERVATION VS. PROPHYLACTIC SELECTIVE LEVEL VI NECK DISSECTION IN PAPILLARY THYROID CARCINOMA

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Background: The indication of prophylactic central neck dissection (level VI) in papillary thyroid cancer is controversial.

Objectives: The aim of this retrospective cohort study was to assess the long-term results of observation vs. prophylactic central neck dissection in patients with papillary thyroid carcinoma.

Patients and Methods: A group of 580 consecutive patients with previously untreated papillary thyroid cancers without lymph node metastasis, as determined by clinical examination and ultrasound (cN0), in addition to having negative macroscopic findings during the surgical procedure, were eligible for the study. A total of 102 patients (Group A) underwent total thyroidectomy with elective central neck dissection, and 478 (Group B) underwent total thyroidectomy alone. Demographic, clinical and pathological features were analyzed. Statistical analysis included the chi-square test, and significance was set at p<0.05.

Results: In Group A patients, the rate of occult metastatic disease was 67.2% (all pN1a). Group A patients were younger; their tumors were larger in size (mean of 14.8 mm versus 10.2 mm in group B; p<0.0001) and they had vascular lymphatic invasion more frequently. More patients in Group A were treated with adjuvant radioiodine and received higher doses. Group A patients exhibited higher rates of temporary hypocalcaemia (47.1% vs. 32.2%; p=0.004) and permanent hypoparathyroidism (12.1% vs. 2.7%; p<0.001). The incidence of temporary and permanent recurrent laryngeal nerve dysfunction was also significantly higher in Group A patients (10.7% vs. 6.0% (p=0.042) and 5.9% vs. 1.4% (p=0.015), respectively). With a mean follow-up of 80.2 months (Group A) versus 67.4 months (Group B), the overall recurrence rate at level VI was 1.9% (11/580) with 3.9% (4/102) in Group A and 1.5% (7/472) in Group B. In Group A patients, all recurrences occurred in the lymph nodes of the lateral chains.

Conclusions: Although the risk of occult lymph node metastasis reaches 67% in a selected group of patients, the elective indication of central compartment dissection for patients with papillary thyroid carcinoma increases the risk of complications and does not contribute to an increase in locoregional control rates.
S116 PATTERN OF NECK RECURRENCE FOLLOWING LATERAL NECK DISSECTION FOR CERVICAL METASTASES IN PAPILLARY THYROID CANCER
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Background:

The objective of this study was to evaluate the pattern of nodal recurrence in patients who underwent a therapeutic lateral neck dissection (LND) for PTC with cervical metastases and to determine if there was any correlation between the extent of initial dissection and pattern of neck recurrence.

Methods:

3664 patients with thyroid cancer managed between 1986 and 2010 at Memorial Sloan-Kettering Cancer Center were identified from our institutional database. Four-hundred eighty-four patients who had a LND with thyroidectomy were included. Patients with non-papillary histology, M1 disease at presentation and those who were considered unresectable were excluded from analyses. Tumor factors, patient demographics, extent of initial LND and adjuvant therapy with radioactive iodine were recorded. LND was categorized into comprehensive LND (CLND) including levels II-V and selective LND (SLND) removing levels with gross disease with or without the addition of at-risk levels. Patterns of recurrent lateral neck metastases by level involvement were recorded and outcomes were calculated using the Kaplan Meier method.

Results:

484 patients were treated with LND for cervical metastases. 281 (58%) patients were female and 203 (42%) male. 209 patients were over 45 years of age (43%). 364 (75%) had a CLND and 120 (25%) patients had a SLND. More pathological lymph nodes were resected in CLND when compared to SLND patients (5.7 vs 3.7, \( p<0.001 \)). Otherwise, there were no significant differences between the CLND and SLND groups in terms of age, gender, type of thyroidectomy, T stage, N stage, size of lymph nodes removed, lymph node burden (ratio of the number of positive nodes to total number of nodes removed), nodes with extracapsular spread, postoperative radiotherapy or radioactive iodine administration. 38 (8%) patients had lateral neck recurrence: 27/364 (7%) CLND and 11/120 (9%) SLND. The average duration of follow-up for each group was 94.3 months (CLND) and 81.1 months (SLND). In CLND patients, 9 recurrences were ipsilateral occurring within the dissected field (9/364=2.5%), 1 was ipsilateral occurring in level 1 (0.2%), 15 (4%) were in the contralateral neck and 2 (0.5%) recurred both within and outside the previous field. In SLND patients, all recurrences (11/120=9%) were ipsilateral occurring within the previously operated field. Seven patients recurred within the previously dissected levels only. Two patients recurred within the previous dissected levels as well as in ipsilateral levels that were not previously dissected. Two patients recurred within the previously dissected levels as well as in the contralateral neck. Therefore, patients who underwent SLND were more likely to recur within the ipsilateral dissected neck (9% vs. 3%, \( p=0.001 \)).

Conclusion:
Patients with cN+ PTC managed by CLND have lower rates of ipsilateral neck recurrence compared to patients managed by SLND. SLND should be reserved for select patients with low volume disease localized to specific neck levels.
Background: The decision to perform a prophylactic central neck dissection (CND) in patients with well-differentiated thyroid cancer (WDTC) remains controversial. Furthermore, once lymph node (LN) metastases are identified in a clinically N0 neck, how this information impacts the decision to administer radioactive iodine (RAI) remains unclear.

Objectives: 1) To assess the indications for performing CND and explore variability of LN retrieval across centers and amongst surgeons in the province of Alberta. 2) To determine factors that predict the use of adjuvant RAI in this population.

Study Design: Province-wide cross-sectional analysis

Methods: A prospectively collected provincial synoptic operative report [WebSMR] identified patients who underwent total thyroidectomy for WDTC. Demographics, peri-operative and pathologic factors were analyzed. Chi-square tests were used for bivariate analysis and logistic regression was used for multivariate analysis. Significance was set at p < .05

Results: Between 2009-2012, 18 surgeons performed 425 CND's, 313 unilateral and 112 bilateral. The mean LN yield was 7.4 +/- 6.3 nodes for unilateral CND and 11.9 +/- 7.5 for bilateral CND. Lymph node yield varied significantly by surgeon as well as by center. 224 CND were prophylactic (no clinically or radiographically apparent LN metastases). Conventional pre-operative risk factors such as age, tumor size, and suspicion of extra-thyroidal extension were not predictors of performing a prophylactic CND. Positive LN's were retrieved in 40% of prophylactic CND, and thus 40% of patients were upstaged from clinical N0 to pathologic N1a stage as a result of performing a CND. Amongst all peri-operative predictors of receiving RAI, the sheer presence of LN metastases was the strongest predictor [OR=5.9(3.7-9.5)]. Tumor size was a modest predictor [OR=1.8(1.5-2.1)] while traditional risk factors for more aggressive WDTC such as age and evidence of extra-thyroidal extension did not predict use of adjuvant RAI. Furthermore, when stratifying the presence of metastatic lymph nodes into 3 groups, as proposed by Randolph et al(1) (no nodes, 1 to 5 nodes, and greater than 5 nodes), patients with greater than 5 nodes were the most likely to receive RAI [OR = 23.3(8.3,65.3)], followed by patients with 1 to 5 nodes identified [OR = 5.9 (3.8,9.3)].

Conclusions: In this provincial cohort, conventional risk factors were not identified as indications for performing a prophylactic CND, implying that the decision varied from surgeon to surgeon and did not follow any specific algorithm. Prophylactic CND upstaged 40% of patients from cN0 to pN1a, and as such these patients were six times more likely to receive adjuvant RAI. Further, patients with greater than 5 metastatic lymph nodes were 23 times more likely to receive RAI. By contrast, conventional risk factors were not predictors of receiving adjuvant RAI.

1. Randoph GW, Duh QY, Keller KS, LiVolsi VA, Mandel SJ, Steward DL, Tufano RP, Tuttle RM. The prognostic significance of nodal metastases from papillary thyroid carcinoma can be stratified based on the size and number of metastatic lymph nodes, as well as the presence of extranodal extension. Thyroid 2012; 22(11): 1144-52.
S122 IMPACT OF LYMPH NODE METASTASES WITH RECURRENT LARYNGEAL NERVE INVASION IN PATIENTS WITH PAPILLARY THYROID CARCINOMA

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Background:

Papillary thyroid carcinoma (PTC) has excellent prognosis. Although rare, PTC invasion in the upper aerodigestive tract affects patient prognosis and quality of life. Lymph node metastases (LNM) to adjacent organs have been encountered during thyroid surgeries. In the central compartment, the recurrent laryngeal nerve (RLN) is most frequently invaded by LNM. RLN invasion by the primary tumor has been reported, whereas RLN invasion by LNM has not.

Objective:

To characterize LNM with RLN invasion in the central compartment in patients with PAC.

Methods:

In this retrospective study, we investigated 38 (6%) patients with 40 RLN invasion (LNM invasion group) and 112 (17.8%) patients with 117 RLN invasion sides in the primary tumor (primary invasion group) from 629 patients with PAC who were initially surgically treated from January 1981 to December 2012.

Results

In all, 70% of the RLN invasions in the LNM invasion group were on the right side, while the frequency of RLN invasion in the primary invasion group was nearly equal. RLN invasion caused paralysis, affecting 13 nerves (32.5%) in the LNM invasion group and 68 nerves (58%) in the primary invasion group. There were significant differences in the frequency of laterality and preoperative RLN paralysis between the two groups. In the LNM invasion group, the longest diameter of metastatic lymph nodes (mean ± SD) in patients with RLN paralysis was 21 ± 8 mm, whereas the diameter in those without RLN paralysis was 14 ± 7 mm. There was a significant size difference in LNM in patients with and without RLN paralysis.

Conclusions

Many patients with RLN invasion via LNM did not have preoperative nerve paralysis, and RLN invasion occurred on the right side. The average ± SD size of LNM with RLN invasion in patients without nerve paralysis was 14 ± 7mm. Lymph nodes > 7mm in the central compartment, as detected on preoperative US, were suggestive of RLN invasion.
LYMPH NODE CHARACTERISTICS PREDICTIVE OF OUTCOME IN PATIENTS WITH THYROID CANCER HAVING A LATERAL NECK DISSECTION
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Background

Previous publications suggest that increasing number, size and ratio of positive lymph nodes in the lateral neck predict poorer outcome in patients with differentiate thyroid cancer (DTC). The objective of our study was to define which lymph node characteristics have prognostic significance in a large cohort of patients with preoperative clinical or radiological evidence of metastatic lymph nodes in the lateral neck.

Methods

An institutional database of 3664 previously untreated patients with DTC operated between 1986 and 2010 was reviewed. Of these, 463 patients had pathological positive lateral neck metastases following a therapeutic neck dissection. The number of positive lymph nodes (LNs), size of the largest LN, ratio of positive LNs to total number of LNs removed (lymph node burden), and presence of extracapsular spread (ECS) were recorded for each patient. Cutoffs for each LN feature were determined by receiver operating characteristic curves for recurrence free survival (RFS) and disease specific survival (DSS) at various cut-points based on maximized sensitivity and specificity. LN variables predictive of RFS and DSS were identified by univariate analyses using the Kaplan-Meier method and multivariate analysis using the Cox proportional hazards model.

Results

The median age was 41.3 years (range 5.4-85.5). The median follow up was 65.1 months (range 1-332). Of the 463 patients, 64 patients had recurrent disease; these were local in 6, regional in 43 and distant in 32 patients. Univariate predictors of RFS were > 10 positive nodes (p=0.011), lymph node burden >20% (p<0.001), and bilateral neck disease (p=0.015). ECS and size of largest LN were not predictive of RFS on univariate analysis. On multivariate analysis, lymph node burden> 20% conferred a HR ratio of 3.089 (p<0.000, 95%CI 1.727-5.527) while neither the number of positive LNs nor the laterality of neck disease were independently predictive of RFS. No lateral LN characteristics were predictive of DSS.

Conclusions

Our data suggests the presence of greater than 20% positive nodes in the lateral neck is a significant predictor for recurrence in patients with DTC.