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ORIGINAL ARTICLE

Risk Factor of Central Lymph Node Metastasis in Papillary Thyroid Microcarcinoma

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ABSTRACT

Background: This study's goals were to assess the cervical central lymph node status and predictive value of SLN biopsy during operate and to identify clinic pathological factors, that were used to be independent predictors for analyzed central lymph node metastasis in papillary thyroid carcinoma.

Study design: This was a cross-sectional study conducted at Sahara Medical College, Narowal for the duration of six months, from July 2022 to December 2022.

Methods: The total N=300 people participated in this study. The participants were split into two groups: positive for cervical central lymph nodes CCLN (n = 210) and negative for cervical central lymph nodes CCLN (n = 90). In cases with positive SLNB, the positive sentinel lymph node ratio and additional positive lymph node (APLN) were examined. Investigators looked into SLNB's effectiveness.

Results: The age range was 24-40 years in which cervical central lymph node case was (57%); p=0.002**. The maximum diameter of tumor (98%) was 3-4 cm show significantly P<0.05. The multiple focus included unilateral (18.3%) and bilateral region (82%) show significant changes P<0.05. According to the tumor locations, the positive case of central lymph node were as following; lower area (20%), middle area (53.3%) and upper area (27%) the difference were significant (p<0.05). The metastatic rate of lymph node was related to SLN (67%) and CCLNM (46%). APLN positive show additional lymph node on cancerous participants. The evaluation of CNM and APLN using the sensitivity, specificity, false positive rates, positive predictive value, and negative predictive value of SLNB.

Conclusion: In participants with positive case reports, age, sex, tumour size, location, extra thyroidal invasion, and capsule involvement were independent risk factors for CLN metastasis. If a positive SLN could be used to predict the presence of APLN, a theoretical basis for intraoperative lymph node dissection might be offered.

Keyword: Metastasis, Tumor size, Multifocality,

INTRODUCTION

The thyroid gland contains nodules, which can be benign or cancerous tumors with different growth patterns. Multinodular goitre is the most common thyroid condition. Thyroid cancer makes up more than 90% of all endocrine cancers worldwide and is the most frequent malignant endocrine tumor. Instead of being a single disease, thyroid cancer is made up of various histologic subtypes that come from various embryological cell types. Additionally, there are a number of genetic variations that set one type apart from another. The majority of thyroid cancers are well-differentiated thyroid carcinomas, a common heterogeneous group that portends higher morbidity and mortality.[1] Poorly differentiated thyroid carcinomas, anaplastic thyroid carcinomas, medullary thyroid carcinomas, particular sarcomas, and primary thyroid teratomas are all included in this diverse group. In addition, newer types have been identified as a result of genetic mutations and origins in embryologic cells. These neoplasms are uncommon, but they still play a significant role in the differential diagnosis of any thyroid mass. Core needle biopsies for rapidly expanding thyroid masses are now thought to be expedient and appropriate in certain situations. [2]

Age-standardized thyroid cancer incidence rates worldwide in 2020 were 10.1/ 100 000 for women and 3/100 000 for men, while age-standardized mortality rates were 0/5 for females and 0/3 for males. While mortality rates varied little between different environments, incidence rates for both sexes were five times higher in high and very high Human Development Index countries than in low and medium Human Development Index countries. Incidence rates for women varied across global regions by more than 15 times. In most countries, mortality rates were less than one per 100,000 for both sexes. The highest incidence-to-mortality rate ratio was found in South Korea, which was followed by Cyprus and Canada.[3]

Thyroid cancer incidence has increased recently, especially for papillary thyroid microcarcinoma, which accounts for 85% to 90% of all thyroid carcinomas. The prevalence of central lymph node metastasis (CLNM), which can range from 40% to 90%, is high in PTC. According to a report, patients with CLNM may have a poorer prognosis and a higher risk of distant metastasis. However, given the postoperative difficulties associated with the abolishment of the CLND, it is questionable as to if CLN surgical intervention should be carried out in all PTC patients. Therefore, from a clinical standpoint, it is crucial to identify patients who are at a high risk for CLNM before surgery. Furthermore, the first site of nodal metastasis for thyroid cancer appears to be the central compartment of lymph nodes. To assess the lymph condition before the procedure, the primary techniques used today were invasive fine needle aspiration (FNA) and ultrasonography (US), which both had low susceptibility. There is still a need for a method that can more correctly assess the risk of cervical lymph node metastasis. It is critical to develop new diagnostic methods for determining the status of cervical lymph nodes.[4, 5]

When a tumor's lymphatic channels cause metastasis, this lymph node ought to be the first one to become involved. The purpose of this study was to evaluate the value of SLN biopsy in patients with papillary thyroid carcinoma as detected by methylene blue (methylthionium chloride). expressed a desire to have their disease removed. Using ultrasound or palpation, all tumors were found.[6]

The data published in 2016 showed that cancer of thyroid gland showed a rapid growth and with a diameter less than 1.0 cm, which accounted for approximately 35% of all thyroid cancers in 1988. Thyroid microcarcinoma, which is present in > 50% of newly discovered cases of cancer, has a favorable prognosis and a 97% 5-year survival rate. The most crucial form of treatment for thyroid carcinoma is still surgery. The use of SLNB to assess the status of the axillary lymph nodes in breast cancer is widely accepted, but there is insufficient data to support its use in papillary thyroid microcarcinoma.[7]

This study's goals were to assess the cervical central lymph node status and predictive value of SLN biopsy during operate and to identify clinic pathological factors, that were used to be

independent predictors for analyzed central lymph node metastasis in papillary thyroid carcinoma.

METHODS

This was a cross-sectional study conducted at Sahara Medical College, Narowal for the duration of six months, from July 2022 to December 2022. The total N=300 people participated in this study. The participants were split into two groups: positive for cervical central lymph nodes CCLN (n = 210) and negative for cervical central lymph nodes CCLN (n = 90). Fine-needle aspiration cytology was used to accurately diagnose papillary carcinoma in each patient prior to surgery, and each patient expressed a desire to have their disease removed. Using ultrasound or palpation, all tumors were found. According to inclusion criteria: Pappilary thyroid cancer with a tumor diameter greater than 4 cm is included. Other cancers, SLN not discovered during surgery, and ineligibility for surgery are all exclusion criteria. Prior to surgery, the written authorization for the operating condition and perioperative frozen pathological evaluation was decided to sign, and the application for the cross-sectional study was signed during the follow-up. All procedures were carried out by surgeons. SPSS 21 was used to analyse the data. The data that was categorical will be presented as frequency and percentage. The p value was 0.05, indicating that the variables had significantly changed.

RESULTS

The demographic data shows the total number of the participants N=300 which divided into two groups CCLN positive (70%) and CCLN negative (30%) cases. Both sex were included female (83.3%) and male (17%). The age range was <24 and >61 years. The thyroid tumor was evaluate on the basis of demographic variables were shown.

Table 1: Demographic variables

Variables	Total No. of participants =N=300	Cervical Central lymph node (CCLN)	Cervical Central lymph node (CCLN)	P value
		Negative case n=90 (30%)	positive case N=210 (70%)	
Sex				<0.01*
Female	250(83.3%)	50(56%)	160(76.1%)	
Male	50(17%)	20(22.2%)	70(33.3%)	
Age				<0.002 **
<24	35(12%)	5(6%)	30(14.2%)	
25-40	170(57%)	10(11.1%)	160(76.1%)	
41-60	75(25%)	10(11.1%)	65(31%)	
>61	20(7%)	8(9%)	12(6%)	
Tumor maximum diameter				<0.001 **
≤ 1-2 cm	15(5%)	10(11.1%)	5(2.3%)	
3-4 cm	250(83.3%)	45(50%)	205(98%)	
>4-5 cm	35(12%)	20(22.2%)	15(7.1%)	
Extrathyroide invassion				=0.004
Yes	115(38.3%)	75(83.3%)	50(24%)	
No	185(62%)	5(6%)	180(86%)	
Capsule involvement				<0.001 **
Yes	140(47%)	75(83.3%)	70(33.3%)	
No	150(50%)	80(89%)	70(33.3%)	
Single focus	145(48.3%)	65(72.2%)	80(38%)	<0.002 **
Multiple focus				<0.001 **
Uniletral	55(18.3%)	40(44.4%)	10(5%)	
Bileteral	245(82%)	50(56%)	195(93%)	
Hashimoto thyroiditis				=0.54
Yes	110(37%)	80(89%)	30(14.2%)	
No	190(63.3%)	40(44.4%)	150(71.4%)	
Complicated with nodular goiter				<0.0001***
Yes	115(38.3%)	80(89%)	35(17%)	
No	185(62%)	10(11.1%)	175(83.3%)	
Symoptoms				<0.01*
Pain	90(30%)	40(44.4%)	50(24%)	
Compression	100(33.3%)	20(22.2%)	80(38%)	
Palpable	110(37%)	40(44.4%)	70(33.3%)	
Tumor area				<0.0001***
Upper	80(27%)	25(28%)	55(26.1%)	
lower	60(20%)	20(22.2%)	30(14.2%)	
Middle	160(53.3%)	25(28%)	135(64.2%)	
Multifocality				0.86
Yes	70(23.3%)	40(44.4%)	20(10%)	
No	230(77%)	80(89%)	150(71.4%)	

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.0; ***p<0.00:

The total number of participants was 300. The female and male ratio was 4:1. The age range was 24-61 years in which cervical central lymph node positive case was (70%); p=0.001** show significantly greater as compared to negative case. The maximum diameter of tumor (98%) was 3-4 cm show significantly higher (p=0.002**). The extrathyriode invasion cases was shown 115(38.3%). The single focus was (48.3%) and multiple focus included unilateral (18.3%) and bilateral region (82%) show significant changes (p=0.002** and 0.001**). The Hashimoto thyroiditis cases was (14.2%; p=0.54). The complicated nodular goiter was 115(38.3%). The symptoms was detected in positive cases (24%) pain, (38%) compression such as dyspenia and dysphagia while (33.3%) participants was detected neck palpable and thickening; (p=0.01*). According to the tumor locations, the positive case of central lymph node were as following; lower area (20%), middle area (53.3%) and upper area (27%) the difference were significant (p<0.0001***). The participants was further investigate on the basis of multifocality but there was non-significant changes (p=0.86) were seen in Table 1

Table 2: To evaluate logistic regression analysis of independent factors.

Parameters	p	Exp (B)	95% CI for Exp (B)	
			lower	upper
Sex	<0.01*	0.71	0.607	0.766
Age	<0.002**	0.81	0.559	0.681
Symptoms	<0.01*	1.268	0.155	1.98
Multifocality	=0.86	2.333	0.921	1.590
Tumor size	<0.001**	2.98	3.33	3.98
Tumor area	<0.0001***	1.52	2.321	4.441
Extrathyriodal invasion	=0.004	3.91	3.111	5.633
Capsule involvemnet	<0.001**	0.89	1.22	2.31
Complicated with nodular goiter	<0.0001***	1.02	0.871	1.991

Mean ± SEM: ANOVA SPS Test* p< 0.0; **p<0.0; ***p<0.00:

The logistic regression model analysis included the age, sex (male and female), symptoms and signs, tumor size, extrathryidal invasion, and complicated with nodular goiter. These were discovered to have an independent impact on participants who had central lymph node positive cases were seen in table 2.

Table 3: To evaluate lymph node of thyroid microcarcinoma.

Lymph node (LN)	LN metastatic	Normal distribution test	Median	Metastatic cases	Metastatic rate (%)
SLN (100)	90	Z=1.567; P=0.001**	4(5, 10)	60	67%
CCLNM (180)	110	Z=1.238; P=0.01*	8(6, 12)	50	46%

The rate of the lymph nodes biopsy was shown in Table 3.

Table 4: To evaluate SLN, CCLN and APLN

SLN	CCLN +ve n= 50	CCLN–ve n=100	APLN+ve n=60	APLN-ve n=80
Positive	40	30	55	45
Negative	10	70	15	35
Sensitivity	72%	28%	53%	57%
Specficity rate	80%	20%	60%	40%
False+ve rate	1	9%	16.1%	0
Positive predictive value	85%	15%	30.9%	70.1%

By postoperative pathological examination, there were a total of 60 cases with sentinel lymph node (SLN) metastasis, 50 cases with central metastasis, and 50 cases of APLN discovered

following surgery but skipped by biopsy. While 55 cases with APLN positive show additional lymph nodes, the 35 cases with ALPN did not. The metastasis rate for SLN was 67% (60/90), while the rate for CCLN was 46% (50/110) and the SLNB-based prediction value for the CCLN and APLN metastasis were shown in Table 4.

DISCUSSION

The most prevalent endocrine cancer is papillary thyroid carcinoma (PTC). It makes up about 85% of thyroid cancers with well-differentiated follicular origin. Even though the majority of PTCs have a high degree of differentiation and a low incidence of local invasion, recurrences and distant metastases, a small subset of tumors exhibit heterogeneity with more aggressive variants that have unique clinical, pathological, and molecular characteristics.[8, 9]

In Our study to found that of 300 participants with positive and negative central lymph node cases were analyzed. The findings showed that, rather than any other poor clinic pathologic characteristics, CCLN metastasis was greater linked with larger tumor size and capsule involvement. Sentinel lymph node 67% biopsy provided a reliable assessment of the condition of the central lymph nodes. The demographic factors such as age, sex, tumor growth, capsular involvement, goiter nodular, and other factors were found to be multivariate analysis in this study. According to several studies, LNM is more common in young patients male or female with larger tumors, and it may be used as a predictor of LNM. The surgical management of PTC may also be impacted by gender. The results of our study, as currently interpreted, indicate that women have a high incidence of cervical central lymph node (CCLN) metastasis positive case (76.1%) which was used as independent predictor of CCLN metastasis (95% class interval [CI]: 0.607-0.766; odd ratio OR=0.71; p<0.01*) in multivariate analysis. We were agree with previous study.[10, 11]

In previous study to show that age was a significant risk factor in several thyroid cancer staging systems. The various studies demonstrate that lymph node metastasis was independently predicted by age 45 years (LNM). Ages under 45 years old had a higher LNM rate.[12, 13] According to our study prediction that the age were divided into three groups and the results show high significant between the age range 25-40 years. The age was used to be independent predictor of CLN metastasis (95% [CI]:0.559-0.681; OR=0.81; P<0.002**). The different age group compared in positive case of CLN metastasis were <24 years (14.2%), 25-40 years (76.1%), 41-60 years (31%) and >61 years (6%). We suggested that it would be beneficial to regularly administer prophylactic CLND to such patients. We were agree with the previous study.[14]

The size of the tumor and extrathyroidal invasion played a critical role in the emergence and development of papillary carcinoma. The effect of tumor size was only felt by patients under the age of 55. A single size cutoff of 2 cm maximized prognostic discrimination, with tumors larger than this measuring five times more likely to recur than those smaller. These results need to be confirmed in distinct, sizable cohorts, and the potential management and staging implications need to be further investigated.[15] In our study, it was found that extrathyroidal invasion-complicated thyroid tumors larger than four cm (83.3%) and smaller than two cm (5%), should not be surgically removed. The prevalence of CLN metastasis positive cases was high in all participants with thyroid nodules 1-2 cm in size and participants complicated by extrathyroidal invasion. A surgical procedure was not used to treat a small tumor. The size of tumor of CLN metastasis (95% [CI]: 3.33-3.98; OR=2.98; P<0.001**) and extrathyroidal invasion (95% [CI]: 3.111-5.633; OR=3.91; P=0.004) was used to independent predictor according to multivariate analysis. We agree with previous study.[16, 17]

Previous research had raised questions about the unclear lymphatic drainage system of the thyroid gland and the connection between the primary tumor site and CCLN metastasis. In our research, we discovered a link between the lymph node metastasis of PTC and the lymph return path in the thyroid region.[18, 19] Multi-focal carcinoma affected various thyroid regions; cases of CLN metastasis were unilateral (5%) and bilateral (93%); p0.001** indicates that the chance of metastasis increased with the number of tumors present. Our prediction was that the tumor area in positive cases would be divided into three regions, with the upper region showing a significant higher p0.0001*** than the lower region (27%), the middle region (53.3%), and the lower region (20%). When the thyroid tumor's upper region was smaller than its middle region, it was more likely to spread if it was there. In multivariate analysis show that tumor location was to be independent predictor for CLN metastasis (95% [CI]: 2.321-4.441; OR= 1.52; P<0.0001***). It also indicate that the middle location of tumor on PTC were significantly higher rate. We were agree with the previous study.[20]

PTC experienced intrathyroidal metastasis, and multifocality was a noteworthy factor. Multivariate analysis results indicate that multifocality was not a reliable indicator of CLN metastasis (p=0.86). Even though PTC had more aggressive characteristics in both multifocality and bilaterally, only multifocality was linked to a higher risk of recurrence. ETE, vascular invasion, CLNM, and LLNM risk all increased with an increase in the number of tumors. In patients without PTMC, multifocality has a strong prognostic value. In the earlier study, we had agree.[21, 22]

CONCLUSION

In participants with positive case reports, age, sex, tumor size, location, extrathyroidal invasion, and capsule involvement were independent risk factors for CLN metastasis. If a positive SLN could be used to predict the presence of APLN, a theoretical basis for intraoperative lymph node dissection might be offered.

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