CLINICAL STUDY

COMPARISON OF LYMPH NODE METASTASIS WITH PREOPERATIVE PALPATION, ULTRASONOGRAPHY, AND COMPUTED TOMOGRAPHY FINDINGS AND POSTOPERATIVE HISTOPATHOLOGICAL RESULTS IN PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA

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SUMMARY

Objective: Lymphatic metastasis is an important prognostic factor in the head and neck cancers. Because of the limitations of physical examination to identify all lymph nodes, radiological imaging modalities (ultrasonography and computed tomography) play a key role. The aim of this study is to compare the relationship between physical examination and radiological imaging modalities and histopathological findings.

Methods: A total of 63 cases who had undergone neck dissection with established diagnosis of head and neck cancer were included in a prospective study. Type of neck dissections, findings of palpation, ultrasonography and computerized tomography were recorded.

Results: There was no statistically significant difference between histopathological findings and palpation (p=0.832), ultrasonography (p=0.523) and computed tomography findings (p=0.581). When ultrasonography, and computed tomography were evaluated in combination, there was no statistically significant difference between histopathological findings, and computed tomography and ultrasonography findings (p=0.581). And also when the three examination findings were evaluated in combination there were no statistically significant difference between histopathological findings, and computed tomography, ultrasonography and palpation findings (p=0.581) either.

Conclusion: Our findings showed that none of the currently available imaging methods are reliable in evaluating the occult regional lymph node metastasis.

Keywords: Head and Neck Lymph Node, Metastasis, Squamous Cell Carcinoma, Histopathology

BAŞ BOYUN KANSERLI HASTALARDA LENF NODU METASTAZININ PREOPERATIF PALPASYON, ULTRASON VE BILGISAYARLI TOMOGRAFI SONUÇLARI ILE POSTOPERATIF HISTOPATOLOJIK SONUÇLARININ KARŞILAŞTIRILMASI

ÖZET

Amaç: Lenfatik metastaz, baş ve boyun kanserlerinde önemli bir prognostik faktördür. Lenf nodlarının tümünü fizik muayenede tespit etmek sınırlı olduğundan dolayı radyolojik görüntüleme yöntemleri (Ultrasonografi ve Bilgisayarlı Tomografi) anahtar rol oynamaktadır. Bu çalışmanın amacı, fizik muayene ve radyolojik görüntüleme yöntemleri ile histopatolojik bulgular arasındaki ilişkiyi karşılaştırmaktır.

Yöntemler: Bu prospektif çalışmaya baş boyun kanseri tanısıyla boyun diseksiyonu yapılmış toplam 63 hasta dahil edildi. Boyun disseksiyon türü ile palpasyon, ultrasonografi ve bilgisayarlı tomografi bulguları kaydedildi.

Bulgular: Histopatolojik bulgularla palpasyon bulguları (p=0.832), ultrasonografi bulguları (p=0.523) ve Bilgisayarlı Tomografi bulguları (p=0.581) arasında istatistiksel olarak anlamlı bir fark görülmedi. Ultrasonografi ve Bilgisayarlı Tomografi birlikte değerlendirildiğinde, histopatolojik bulgularla Ultrasonografi ve Bilgisayarlı Tomografi bulguları arasında istatistiksel anlamlı fark görülmedi (p=0.581). Ayrıca üç muayenenin bulguları bir arada değerlendirildiğinde de histopatolojik bulgularla Bilgisayarlı Tomografi, ultrasonografi ve palpasyon bulguları arasında istatistiksel olarak anlamlı fark bulunmadı (p=0.581).

Sonuç: Bu çalışma göstermiştir ki, günümüzde geçerli olan görüntüleme yöntemlerinin hiçbirisi okkült rejyonel lenf nodu metastazını değerlendirmede güvenilir değildir.

Anahtar Sözcükler: Baş ve Boyun Lenf Nodu, Metastaz, Squamoz Hücreli Karsinom, Histopatoloji

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INTRODUCTION

Head and neck cancers constitute nearly 5 % of all cancers, and their frequency increases worldwide.[1] Most of these cancers are squamous cell cancers (SCC), and originate from squamous epithelium of upper gastrointestinal and respiratory tract.[2]

Lymphatic metastasis is an important prognostic factor in patients with SCC of the head

and neck.[3] Only physical examination with palpation is not sufficient to discriminate between benign and malign lymph nodes. Even on superficial areas as cervical region, physical evaluation does not determine the metastasis reliably.[4] Since deeply-localized lymph nodes cannot be sensed, palpation has higher false-negativity rates. Besides, palpation might fail in patients who had been previously operated or received radiotherapy, and also in obese, and short-necked patients. Besides it has limitations as inability to identify very deeply or retropharyngeal located lymph nodes.[5]

In addition to these limitations of physical examination, ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), fine needle biopsy under the guidance of ultrasonography, lymphoscintigraphy, elastography, and positron emission tomography (PET) have been used in the evaluation of the lymph node status in patients with head and neck cancers. Radiological imaging modalities play a key role in the determination of surgical treatment model. However occasionally, we encounter some patients in whom these methods are not satisfactory or misleading.

The aim of this study is to histopathologically evaluate cervical lymph nodes during the postoperative period which could be or could not be identified in the preoperative period in patients with squamous cell cancers of head and neck, and also to measure diagnostic power of radiological imaging modalities.

MATERIAL and METHODS

This study was realized in the Clinics of Ear, Nose, Throat Diseases and Head and Neck Surgery, Ankara Ataturk Training and Research Hospital between February 2005, and July 2012. A total of 83 cases (42 males, 41 females) with a median age of 56 (26-80 yrs.) years who had undergone neck dissection with established diagnosis of head and neck cancer were included in the study. Cases who had previously undergone neck dissection, radiotherapy or chemotherapy were excluded from the study. Distribution of the cases according to primary tumoral foci is shown in Table 1.

Unilateral (n=65, 78.3 %), and bilateral (n=18, 21.7 %) neck dissections were performed. Unilateral neck dissections were as functional (n=25, 38.5 %), radical (n= 14, 21.5 %), modified radical (n=3, 5.6 %) and selective (n=23, 34.4 %) neck dissections, while bilateral neck dissections were as functional (n=10, 55.6 %), and selective (n=8, 44.4 %) neck dissections. Selective neck dissections included bilateral (n=8, 25.8 %), and unilateral (n=20, 64.5 %) supraomohyoid neck dissections (levels 1, 2, and 3) and 3 of these patients (9.7 %) underwent unilateral posterolateral neck dissections (levels 2, 3, 4, and 5).

Preoperative physical examination with palpations of head and neck area of all patients were performed by the same physician. If palpated lymph nodes were solid, painless, and fixed with a diameter of > 1.5 cm, then they were evaluated as malignant lymph nodes, and their characteristic features were noted. Then examinations with US (8 MHz Linear Probe, Mindray Medical Systems, China) and CT (Toshiba Aquilion 64 Multislice, Japan) were performed, and their relevant data were recorded. Criteria of malignancy of the visualized lymph nodes (if any) including their dimensions, configurations, hilar anatomy, contours, cortical thickness, echogenicities, vascular patterns, and also the presence of necrotic areas, and calcifications were assessed. Based on these characteristic features, lymph nodes were divided into two categories; reactive, and malignant.

Following neck dissection, histopathological examinations of the lymph nodes harvested from specimens containing neck lymphatics were performed. Histopathological materials were re-examined based on the classification recommended by American Joint Cancer Committee (AJCC) 2010 reports by the time.[6] Histopathological results were compared with preoperative physical, US, and CT examination findings.

Statistical Analysis

Fundamental statistics summarized demographic and clinical characteristics of the patients. Numerical parameters were concisely expressed as means ± SD, and categorical variables as numbers, and percentages. In secondary comparisons, kappa test was used to determine the concordance between measurement methods, and relevant differences were assessed using McNemar test. For comparisons, 17th version of SPSS program was employed. $p<0.05$ was accepted as the level of significance.

Table 1: Distribution of the cases according to primary tumoral foci

Primary Tumoral Foci	n (%)
Larynx Carcinoma	25 (29.4)
Hypopharynx Carcinoma	4 (4.7)
Oral Cavity Carcinomas	
Lip Carcinoma	19 (22.4)
Tonque Carcinoma	12 (14.1)
Gingival Carcinoma	1 (1.2)
Retromolar Trigon Carcinoma	1 (1.2)
Carcinoma of the oral cavity base	1 (1.2)
Oropharynx Carcinoma	
Tonsil Carcinoma	1 (1.2)
Salıvary Gland Carcinoma	
Parotid Carcinoma	2 (2.4)
Auricular Carcinoma	1 (1.2)
Middle Ear Carcinoma	1 (1.2)
Nasal Cavity Carcinoma	2 (2.4)
Thyroid Carcinoma	13 (15.3)

RESULTS

On physical head and neck examination of the patients, bilateral (n=9, 10.6 %), and unilateral (n=16; 18.8 %) palpable lymph nodes were detected, while in 58 (70.6 %) patients had any lymph nodes could not be palpated. Histopathologically examination of the palpable lymph nodes of 25 cases were reported as metastatic (n=15, 60%), and reactive (n=10, 40 %) lymph nodes. Histopathological examinations of the preparations of 58 cases who had impalpable lymph nodes, were reported as metastatic (n=12, 20.6 %), and reactive (n=46, 79.4 %) lymph nodes (Table 2). The diagnostic value of palpation in the detection of metastatic lymph nodes yielded true-positive (n=15), true-negative (n=46), false-positive (n=10), and false-negative (n=12) results (Table 2). In the light of these results, sensitivity (55 %), specificity (82 %), positive (60%), and negative (79 %) predictive values, and accuracy rates (73 %) of palpation in the detection of metastatic lymph nodes were also calculated (Table 3). A statistically significant difference was not detected between histopathologically, and palpation findings (p=0.832).

All of the palpable lymph nodes of 25 patients detected on physical examination were also observed on US. Twenty seven of 58 patients (46.5 %) with impalpable lymph nodes, US revealed the presence of lymph nodes. Histopathologically examination revealed reactive (n=9), and metastatic (n=18) lymph nodes. Examination with US detected lymphadenomegaly in 52 (62.6 %) of 83 patients (Table 4). Twenty one of 52 (41.2 %) patients had bilateral lymphadenomegaly. Among 52 patients, 31 cases (37.3%) had apparently metastatic and 21 patients (62.7 %) had reactive lymphadenomegaly (Table 4). Postoperative histopathologically evaluation revealed the presence of metastatic lymph nodes in 11 (34.4 %) of 32 patients in whom US, and palpation could not detect lymphadenomegaly (Table 4). In 9 (17.3 %) of 52 patients whose US findings were reported as reactive lymphadenomegaly, postoperative histopathologic evaluation detected evidence of metastatic lymph node. Postoperative histopathological evaluation of the specimens of 18 (58 %) out of 31 patients which were reported as metastatic lymphadenomegaly in US, disclosed metastatic lymph nodes, and reactive lymphadenomegaly (42%) in the remaining 13

patients (Table 4). US assessments revealed true-positivity (n=18), true-negativity (n=43), false-positivity (n=13), and false-negativity (n=9) of the results in respective number of patients (Table 4). Sensitivity, specificity, positive, and negative predictive values, and degree of accuracy of ultrasonographic examinations in the detection of metastatic lymph nodes were estimated as 66, 76, 58, and 82, and 73 %, respectively (Table 3). A statistically significant difference was not found between histopathologically, and US findings (p=0.523).

Lymphadenomegaly detected in 83 patients by CT were of metastatic, and reactive type in 24 (28.9 %), and 59 (71.1 %) cases, respectively. Postoperative histopathological examinations of 59 patients with reactive lymphadenomegaly as assessed by CT, revealed evidence of metastatic lymph nodes in 8 (13.5 %) cases. Metastatic lymph nodes were found in postoperative histopathological examination of 19 (79.1 %) out of 24 patients whose CT reports indicated metastatic lymphadenomegaly (Table 5). US examination of the patients whose CT images suggested metastatic lymphadenomegaly, revealed the presence of reactive (n=14, 58.3 %), and metastatic (n=10, 41.7 %) lymph nodes (Table 5). In one patient, US diagnosis of pathologic lymphadenomegaly was emphasized by CT as reactive lymphadenomegaly. However histopathological report of the same case indicated metastatic lymphadenomegaly. CT examination had demonstrated true-negativity (n=51), true positivity (n=19), false-positivity (n=5), and false- negativity (n=8) in indicated number of cases (Table 5). Sensitivity, specificity, positive, and negative predictive values, and accuracy rate of the CT for the detection of metastatic lymph nodes were estimated as 70, 91, 79, 86, and 84 %, respectively (Table 3). A statistically significant difference was not found between histopathologically, and CT findings (p=0.581).

When US, and CT were evaluated in combination, true-positivity, true-negativity, false-positivity, and false-negativity were detected in 18, 43, 5, and 6 cases, respectively (Table 6). The sensitivity, specificity, positive, and negative predictive values, and accuracy rate of combined US, and CT examinations in the detection of metastatic lymph nodes were 69, 89, 78, 84, and 82 %, respectively (Table 3). A statistically significant difference was not found between histopathologically, and combination of US, and CT findings (p=0.581).

When palpation, US, and CT were evaluated in combination true-positivity (n=15), true-negativity (n=43), false-positivity (n=15), and false-negativity (n=8) were detected in number of cases as stated in parentheses (Table 7). Sensitivity, specificity, positive, and negative predictive values, and accuracy rate of palpation, US, and CT in combination in the detection of metastatic lymph node were calculated as 65, 89, 75, 84, and 81 %, respectively (Table 3). A statistically significant difference was not revealed between histopathologically, and combination of palpation, US, and CT findings (p=0.581).

Table 2: Histopathologic examination of lymph nodes according to palpation

	Histopatholgy	
Palpabl lymph node	Metastatic	Reactive
Lymphadenomegaly (+) (25)	15 (TP)	10 (FP)
Lymphadenomegaly (-) (58)	12 (FN)	46 (TN)

TP(True Positive), TN(True Negative), FP(False Positive), FN(False Negative)

Table 3: Rates (%) of sensitivity, specificity, positive and negative predictive values and accuracy

Methods / **Statistics**	**Palpation**	**US**	**CT**	**US+CT**	**Palpation+ US + CT**
Sensitivity	55	66	70	69	65
Specificity	82	76	91	89	89
Positive Predictive Value	60	58	79	78	75
Negative Predictive Value	79	82	86	84	84
Accuracy Rate	73	73	84	82	81

Table 4: Histopathologic evalution of US detected lymphadenomegaly

Histopathology	Metastatic	Reactive
Ultrasonography		
Pathologic Lymphadenomegaly (31)	18 (TP)	13 (FP)
Reactive Lymphadenomegaly (52)	9 (FN)	43 (TN)

TP(True Positive), TN(True Negative), FP(False Positive), FN(False Negative)

Table 5: Histopathologic evaluation of CT detected lymphadenomegaly

Histopathology / CT	Metastatic	Reactive
Pathologic Lymphadenomegaly (24)	19 (TP)	5 (FP)
Reactive Lymphadenomegaly (59)	8 (FN)	51 (TN)

TP(True Positive), TN(True Negative), FP(False Positive), FN(False Negative)

Table 6: Comparison of histopathologic findings with US+CT detected lymph nodes

Histopathology / USG + BT	Metastatic	Reactive
Pathologic Lymphadenomegaly (23)	18 (TP)	5 (FP)
Reactive Lymphadenomegaly (51)	8 (FN)	43 (TN)

TP(True Positive), TN(True Negative), FP(False Positive), FN(False Negative)

Table 7: Comparison of histopathologic findings with Palpation+US+CT detected lymph nodes

	Histopathology	
Palpation + US + CT	Metastatic	Reactive
Pathologic Lymphadenomegaly (20)	15 (TP)	5 (FP)
Reactive Lymphadenomegaly (51)	8 (FN)	43 (TN)

TP(True Positive), TN(True Negative), FP(False Positive), FN(False Negative)

DISCUSSION

Detection of cervical lymphadenomegaly in cases with head and neck cancer is the most important factor in the prediction of prognosis of these patients.[7] Therefore, the presence of a cervical lymphadenomegaly has an important impact on the treatment regimen. We had the opportunity to compare three fundamental diagnostic methods used currently.

Palpation which is the mostly practicised, but the least reliable method based on the assessments of the physicians. Stell et al. reported lack of any tumoral invasion in 20-40 % of the patients with non –palpable, and 25-50 % of palpable lymphadenomegalies.[8] In our study 25 (30.1 %) of our 83 patients, palpable lymph nodes, and in 15 (60%) these 25 patients metastatic lesions were found. In 20.6 % of the patients with impalpable lymph node enlargement, histologically detected tumoral invasion was found, while in 40 % of the cases with palpable lymphadenopathies, tumoral invasion was not observed. In a similar study by Akoglu et al sensitivity, specificity, positive, and negative predictive values, and accuracy rates of detecting a metastatic lymph node during physical examination were reported as 59, 92, 94, 54, and 70 %, respectively.[4] In our study, sensitivity, specificity, positive, and negative predictive values, and accuracy rates of detecting a metastatic lymph node were estimated as 55, 82, 60, 79, and 73 %, respectively. When these two studies were compared, lower rates of specificity, sensitivity, and positive predictive, but higher negative predictive values were obtain in our study. A statistically significant difference was not found between histopathologic, and palpation findings (p=0.832). Accuracy rate was estimated as 73 %.

In the detection of lymph node enlargement in the patients with head and neck cancers, US has advantages in that is a less-costly, easily applicable, noninvasive method superior to CT in Level I-IIA lesions which does not expose the patients to deleterious effects of radiation.[9] However, it has many disadvantages. For example, US can hardly detect retropharyngeal lymph nodes which are masked by bony structures, and pharyngeal air column.[9] Similarly, upper 1/3 internal jugular, retropharyngeal, and tracheoesophageal lymph nodes are superimposed by bony, and respiratory system organs cannot be satisfactorily evaluated by US[9]. Besides, it is not possibe to reliably discriminate larger reactive lymph nodes from metastatic nodes.[10]

In our study when all criteria were used in combination, sensitivity, specificity, positive, and negative predictive values, and accuracy rate of US were calculated as 66, 76, % 58, 82, and 73 %, respectively. Righi et al reported sensitivity, specificity, positive, and negative predictive values, and accuracy rate of US as 60, 78, 54, 82, and 72 %, respectively.[11] In a similar study by Hohlweg-Majert et al, relevant sensitivity, specificity, positive, and negative predictive values for US were indicated as 74, 91, 66, and 93 % respectively.[9] Still in a

comparable study by Yoon et al, sensitivity, specificity, positive, and negative predictive values, and accuracy rate of US were stated to be 78, 98, 92, 95, and 94 %, respectively.[12] In a study performed in our country, Akoglu et al estimated rates of sensitivity, specifity, positive, and negative predictive values, and accuracy as 81, 64, 81, 64, and 75 %, respectively.[4] In the literature reviews, sensitivity, and specificity of US in the detection of metastatic lymph node enlargement in patients with head and neck cancers have ranged between 44-94%, and 67-100 %, respectively. In our study, rates of specificity and sensitivity for US are in accordance with the literature findings. In our study a statistically significant difference was not found between histopathologic, and US results (p=0.523). However, accuracy rate was estimated as 73 %.

Contrast uptake pattern observed in CT, is helpful in differentiating between inflammatory, and metastatic lymph nodes. Besides the presence of focal defect, and peripheral contrast enhancement are characteristic findings in favour of malignancy even in normal-sized lymph nodes. Round lymph nodes, lymph node conglomerates, indistinct contours, sizes larger than 15 mm, ring-shape contrast uptake, and focal defects in contrast-enhanced areas suggest malignancy.[13] In our study when all criteria were used in combination, sensitivity, specificity, positive, and negative predictive values, and accuracy rate for CT were estimated as 70, 91, 79, 86, and 84 %, respectively. Righi et al reported sensitivity, specificity, positive, and negative predictive values, and accuracy rate of CT as 60, 100, 100, 85, and 87 %, respectively.[10] In a study by Hohlweg-Majert et al sensitivity, specificity, positive, and negative predictive values of CT were reported as 60, 90, 74, and 92 %, respectively.[9] In separate studies conducted by Yoon et al and Akoglu et al sensitivity (77 vs. 77 %), specificity (99 vs. 85%), positive (96 vs. 91 %), and negative (95 vs. 96) predictive values, and accuracy rates (95 vs. 80%) were also reported.[4,12] Karaman et al stated sensitivity, specificity, positive, and negative predictive values of CT as 81, 90, 82, and 90 %, respectively.[14] In the literature reviews, sensitivity, and specificity of CT have been indicated as 59-97 %, and 81-94 %, respectively. In our study sensitivity and specificity of CT are in accordance with the literature. We did not detect a statistically significant difference between histopathologically, and CT findings (p=0.581). Accuracy rate was estimated as 84 %.

When CT, and US are evaluated in combination, Yoon et al reported rates of sensitivity, specificity, and also positive and negative values, and accuracy rate as 78, 99, 96, 95, and 95 %.[12] In our study sensitivity, specificity, positive, and negative predictive values, and accuracy rate of combined evaluation of CT and US combination were 69, 89, 78, 84, and 82 %, respectively. A statistically significant difference was not found between histopathologically, and CT and US combination findings (p=0. 581). Accuracy rate was estimated as 82 %.

Generally the neck dissection was performed only when the presence of metastatic lymph nodes were suspected on the basis of imaging modalities. This is the limitation of these kinds of studies. So, if the lymph nodes were unsuspicious neck dissections were not performed and these were excluded from the analyses. This could be accepted as a selection bias also in our study too.

CONCLUSION

Our results showed that sensitivities and specifities of palpation, US, and CT appeared to be similar in detection of metastatic lymph node detection in patients with SCC of the head and neck. Combination of palpation, US and CT yielded no improved sensitivity and specifity compared with the single use of these techniques. However, preoperative USG and CT scanning of the neck by an experienced radiologist are essential and useful for diagnosis, staging, and therapy choices.

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