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THE RELATIONSHIP BETWEEN LYMPHEDEMA AFTER AXILLARY DISSECTION FOR MALIGNANT SKIN TUMORS OF UPPER EXTREMITY AND NUMBER OF LYMPH NODES REMOVED

ÜST EKSTREMİTE KAYNAKLI MALİGN DERİ TÜMÖRLERİNE YÖNELİK YAPILAN AKSİLLER DİSEKSİYON SONRASI GELİŞEN LENFÖDEM İLE ÇIKARILAN LENF NODU SAYISI ARASINDAKİ İLİŞKİ

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ABSTRACT

Objective: Skin cancers are the most common malignant cancers. For the surgical treatment of skin cancer, there are cases where axillary dissection should be performed, and secondary lymphedema after axillary dissection is not uncommon. The study examined the number of lymph nodes removed in the dissection materials to evaluate the factors that may predict the development of lymphedema.

Material and Method: Our study included patients who underwent axillary lymph node dissection for malignant skin tumors originating from the upper extremities between 2019 and 2022. Age, gender, type of primary malignancy, localization of the lesion, total number of lymph nodes removed in the dissection material, number of metastatic lymph nodes detected in the dissection material, history of SLNB, and the difference in measurements between the operated and non-operated extremity were recorded preoperatively and at the first year postoperatively.

Result: In our study, there was a statistically significant positive correlation between the total number of lymph nodes removed and the diameter difference between the dissected and non-dissected arms. At the same time, there was a statistically significant positive correlation between the number of metastatic lymph nodes and the diameter difference between the dissected limb and the metacarpophalangeal joints of the other limb.

Conclusion: Lymphedema is a complication that is difficult to treat and whose prognosis can be alleviated if detected early. By evaluating the number of excised and metastatic lymph nodes

ÖZET

Amaç: Deri kanserleri en sık görülen malign kanserlerdendir. Cilt kanserinin cerrahi tedavisi için aksiller diseksiyon yapılması gereken durumlar mevcuttur ve aksiller diseksiyon sonrası sekonder lenfödem nadir değildir. Çalışmada, lenfödem gelişimini öngörebilecek faktörleri değerlendirmek için diseksiyon materyallerinde çıkarılan lenf nodu sayısı incelenmiştir.

Gereç ve Yöntem: Çalışmamıza 2019-2022 yılları arasında üst ekstremite kaynaklı malign deri tümörü nedeniyle aksiller lenf nodu diseksiyonu yapılan hastalar dahil edildi. Yaş, cinsiyet, primer malignite tipi, lezyonun lokalizasyonu, diseksiyon materyalinde çıkarılan toplam lenf nodu sayısı, diseksiyon materyalinde saptanan metastatik lenf nodu sayısı, SLNB öyküsü, opere edilen ve edilmeyen ekstremite arasındaki ölçüm farkı preoperatif ve postoperatif birinci yılda kaydedildi.

Bulgular: Çalışmamızda, çıkarılan toplam lenf nodu sayısı ile diseke edilen ve edilmeyen kol arasındaki çap farkı arasında istatistiksel olarak anlamlı pozitif korelasyon bulunurken, metastatik lenf nodu sayısı ile diseke edilen uzuv ile diğer uzvun metakarpofalangeal eklemleri arasındaki çap farkı arasında istatistiksel olarak anlamlı pozitif korelasyon bulunmuştur.

Sonuç: Lenfödem, tedavisi zor olan ve erken teşhis edildiğinde prognozu hafifletilebilen bir komplikasyondur. Diseksiyon materyallerinde eksize edilen lenf nodu sayısı ve metastatik lenf nodu sayısı değerlendirilerek lenfödem gelişebilecek hastalarda erken önlem almak, hastaları eğitmek, bireysel tedavi

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in the dissection materials, it may be possible to take early precautions, educate patients, develop individual treatment modalities, and avoid unwanted complications in patients who may develop lymphedema.

Keywords: Axillary lymph node dissection, melanoma, secondary lymphedema, non-melanoma skin cancer

modaliteleri geliştirmek ve istenmeyen komplikasyonlardan kaçınmak mümkün olabilir.

Anahtar Kelimeler: Aksiller lenf nodu diseksiyonu, melanom, sekonder lenfödem, melanom dışı cilt kanseri

INTRODUCTION

Skin cancer is the most common type of malignancy in the world, and its incidence is significantly increasing (1). Skin cancer types are classified as melanoma and nonmelanoma skin cancers (NMSC). Basal and squamous cell carcinoma are the main forms of NMCS (2). The etiologic factors for skin tumors are multifactorial; thereby, the mechanistic pathways differ. Nevertheless, significant factors include UV radiation, leading to genetic mutation (3).

Treatment modalities vary by the type of skin tumors, and they can be treated by surgery, chemotherapy, or radiotherapy. The gold standard for the management of skin cancer is surgical excision with histopathological control of excision margins (3).

Sentinel lymph node biopsy (SLNB) and regional lymph node dissection are complementary treatment modalities for managing SCCs and melanomas. SCC of the skin has low incidence rates of nodal metastasis. Therefore, regional lymphadenectomy is generally not recommended in clinically node-negative patients (4). In the case of lymph node involvement by SCC, regional lymph node dissection should be preferred. Patients who have melanomas should be investigated for the stage of the disease. When the disease is in its early period, wide surgical excision and the evaluation of the lymph nodes are the essential steps for managing the disease. Patients with clinically node-negative stage I or II melanoma that is 0.8 mm in thickness and located on the trunk or extremities should be allowed to discuss SLNB to provide staging and prognostic information (5). In the case of SLN positivity, completion lymph node dissection (CLND) is performed (6). Axillary, cervical, or inguinal completion lymph node dissection is performed after SLN positivity detection or clinically node-positive situations for metastatic skin tumors. CLND for the skin tumor is a curative process that aims to remove all lymph nodes and metastatic disease in a lymphatic basin. CLND helps to eliminate regional lymph node recurrences and the associated morbidity (7).

Lymphedema is a severe complication for the patient who is already trying to cope with the diagnosis of cancer. Physiologically and psychologically, disturbances will appear during the management of the lymphedema. After all, chronic lymphedema may lead to recurrent infection and even the development of lymphangiosarcoma (8). Postoperative lymphedema following axillary dissection has been studied in depth for breast cancer patients. Hence, while describing the risk factors for lymphedema after axillary dissection, breast cancer-related lymphedema studies must be investigated. Even though the operative techniques are different, the risk factors will be similar. Age, BMI, radiotherapy, sex, race, stage, diabetes, chemotherapy, and number of nodes removed are some of the main risk factors for lymphedema development after axillary dissection due to breast cancer (9).

In this study, we aim to evaluate the risk factors for the development of lymphedema in patients who underwent axillary lymph node dissection (ALND) due to upper extremity skin tumors. In addition, the study aims to evaluate the association between the number of nodes removed during dissection and postoperative lymphedema development. This study retrospectively examines pathology records in patients with ALND, and during follow-ups, our team evaluates lymphedema development by measuring arm circumferences.

MATERIALS and METHODS

In this study, patients who underwent axillary lymph node dissection (ALND) for malignant skin tumors originating from the upper extremities between 2019 and 2022 in the Plastic, Reconstructive, and Aesthetic Surgery Department were included. The study included patients who underwent ALND for cutaneous malignant tumors originating from the upper extremities in our clinic, who were followed up at the physical therapy and rehabilitation center for the prevention of lymphedema in the postoperative period, and in whom we measured the circumference of the relevant upper extremity in the first postoperative year. Exclusion criteria included having undergone ALND in a center other than our clinic, being under 18 years of age, having a history of preoperative trauma or infection in the relevant upper extremity, not attending postoperative follow-up for various reasons (comorbidity, death due to existing disease, etc.), and having undergone ALND for cutaneous malignant tumors located in regions other than the upper extremities (thorax, periumbilical region, etc.).

Patient's age, gender, type of primary malignancy, primary location of the lesion, total number of removed lymph nodes in the dissection material, number of positive lymph nodes detected in the dissection material, history of SLNB, and the difference in measurements between the operated and non-operated extremities in centimeters were recorded preoperatively and at the first year postoperatively. Circumferences of the bilateral arms (15 cm proximal to the elbow), forearms (10 cm distal to the elbow), wrists, and metacarpophalangeal (MCP) joints level were measured in centimeters two weeks before the operation and recorded on a chart. After the operation, a compression garment was applied to the relevant extremity on the first postoperative day, and rehabilitation was performed to prevent lymphedema. Circumferences were measured in centimeters at the bilateral arms (15 cm proximal to the elbow), forearms (10 cm distal to the elbow), wrists, and MCP joints level and recorded on the chart at the first postoperative year. Patients were instructed to refrain from activity before measurement. No patient received radiotherapy after the study.

Axillary lymph node dissection surgery involved removal of level 1-2-3 lymph nodes in the axillary region, while the long thoracic and thoracodorsal nerves were preserved. The total number of lymph nodes removed during the operation and the number of positive lymph nodes were recorded by reviewing the previous medical pathology report records.

The normality assumption of continuous variables was tested by the Shapiro-Wilk test. Categorical variables were presented as frequency (%), and continuous variables were presented as mean±SD, median, and range. Comparisons between two groups in continuous variables were performed with the Mann-Whitney U test. The Spearman correlation test analyzed the level of correlation between two continuous variables. Statistical calculations were performed with SPSS software version 25 (IBM Corp., Armonk, NY, USA). Results were evaluated at a 95% confidence interval, and significance was evaluated at $p<0.05$.

The study protocol was approved by the Medical Ethics Committee of Istanbul University (Date: 17.03.2023 No: 06). All data was anonymized, and the informed consent for every patient was recorded.

RESULTS

This study included 16 patients who underwent axillary lymph node dissection (ALND) for malignant skin tumors originating from upper extremities between 2019 and 2022 in our Plastic, Reconstructive, and Aesthetic Surgery department. Considering the exclusion criteria and the survival rate following melanoma disease, the number of patients included in the study was reduced to eight. The study included eight patients with skin tumors, five males and three females, with a mean age of 63.1±6.9 (Range: 52-73) years. The lesion was localized in the hand in three, forearm in two, arm in two, and axilla in one of the patients. Sentinel lymph node biopsy was performed in four patients, and axillary lymph node dissection was performed in all patients (100%). In axillary lymph node dissection, a mean of 23.4±6 (Range: 14-35) lymph nodes were removed, and carcinoma metastasis was detected in five patients. Lymphedema was observed in four patients during clinical follow-up, with a mean difference of 1.38±1.30 cm (4.4%) between the dissected and the other extremity (Table 1). The circumference measurement results of the patients are presented in detail in Table 2.

There was a statistically significant positive correlation between the number of lymph nodes removed and the diameter difference between the dissected and non-dissected arm ($r=0.734$; $p=0.038$), while there was a statistically significant positive correlation between the number of metastatic lymph nodes and the diameter difference between the dissected extremity and the MCP joints of the other extremity ($r=0.889$; $p=0.044$) (Table 3).

Table 1: Patients' demographic characteristics

Variables (n=8)	**n (%)**
Age, mean (SD)	63.1 (6.9)
Gender	
Male	5 (62.5)
Female	3 (37.5)
Localization of the lesion	
Hand	3 (37.5)
Forearm	2 (25)
Arm	2 (25)
Axillary region	1 (12.5)
SLNB prior to ALND	
Yes	4 (50)
No	4 (50)
Total number of removed lymph nodes, mean (SD)	23.4 (6.0)
Pathological lymph nodes	
Negative	3 (37.5)
Positive	5 (62.5)
Lymphedema	
Yes	4 (50)
No	4 (50)

SLNB: Sentinel lymph node biopsy, ALND: Axillary lymph node dissection, SD: Standard deviation

Table 2: Circumferential difference between operated and non-operated extremities and joints

Circumference measurements	Mean (SD)	Median	Min.-Max.
Arms (cm)	1.38 (1.30)	1	0-4
Forearms (cm)	0.75 (0.707)	1	0-2
Wrists (cm)	0.50 (0.756)	0	0-2
MCP joints (cm)	0.50 (0.535)	0.5	0-1

SD: Standard deviation, MCP: Metacarpophalangeal

Table 3: The relationship between the measurements and total number of removed lymph nodes and total number of metastatic lymph nodes

	TNRLN		TNMLN	
Variables	**r**	**p-value**	**r**	**p-value**
Arms (cm)	**0.734**	**0.038***	-0.433	0.467
Forearms (cm)	0.494	0.213	-0.148	0.812
Wrists (cm)	0.070	0.868	0.344	0.571
MCP joints (cm)	-0.112	0.792	**0.889**	**0.044***

*p<0.05, r: Spearman correlation test, TNRLN: Total number of removed lymph nodes, TNMLN: Total number of metastatic lymph nodes, MCP: Metacarpophalangeal

In patients who underwent SLNB prior to ALND, no significant changes were found in postoperative follow-up circumferential measurements at the arm (p=0.549), forearm (p=0.343), wrist (p=0.405) and MCP joint (p=1.000) level.

DISCUSSION

Skin tumors are common malignancies that require close follow-up after treatment. Our study evaluated the development of lymphedema after axillary dissection, one of the treatment modalities for skin tumors. In our patient group, a significant positive correlation was found between the diameter difference at the arm level of the extremity in which axillary dissection was performed for cutaneous malignant tumor in the upper extremity and the other extremity, as well as the total number of lymph nodes removed in the dissection material. There was also a statistically significant positive correlation between the number of metastatic lymph nodes found in the dissection material and the diameter difference between the MCP joints of the dissected extremity and the other extremity.

Depending on the subtype of skin tumor and the patient's clinical findings, there may be cases where SLNB should be performed before ALND. In the study group, some patients underwent SLNB before ALND; there was no significant difference between the circumferential measurements of the relevant extremity in these patients compared to patients who did not undergo SLNB, and the history of SLNB before dissection did not affect the outcome.

While the number of patients included in our study was 16 in the first phase, the number of patients followed up in the first postoperative year decreased to eight due to the effect of the survival of patients with melanoma, an aggressive skin tumor, and the death of patients due to additional comorbidities, etc. These factors led to a limited number of patients being analyzed. All patients were followed up in physical therapy centers to prevent lymphedema in the postoperative period, and appropriate compression garments were applied. Despite close physical therapy follow-up, a difference in diameter between the extremities with and without dissection was observed.

In the literature, there are studies evaluating lymphedema developing in patients who underwent axillary dissection for breast cancer. In these studies, when the risks for the development of lymphedema were examined, it was observed that the number of resected lymph nodes and the number of pathological lymph nodes were risk-increasing factors (10, 11). In a study conducted for melanoma treatment, it was observed that the total number of resected lymph nodes and the number of pathological lymph nodes were not associated with an increased prevalence of lymphedema. The same study observed that the history of SLNB was not a risk-increasing factor in the development of lymphedema (8). Our study observed that a history of SLNB did not increase the risk of lymphedema after ALND. However, the correlation between the total number of lymph nodes removed, the number of metastatic lymph nodes, and limb diameter differences resulted in different results from the aforementioned study.

Lymphedema is a severe complication after ALND and can be difficult to treat. While cellulitis caused by lymphedema is the main complication, there is a spectrum of complications extending to lymphangiosarcoma, and physiological and psychological disorders are also frequently observed in these patients (12). It is important to take precautions to reduce the development of lymphedema in the early postoperative period. For this purpose, necessary lymphedema training can be tailored individually and by cancer treatment (13). In our study, we focused on the factors we can evaluate in the early period regarding lymphedema development. The pathology report document examined in our outpatient clinic during the postoperative follow-up period was aimed at predicting the development of lymphedema and taking necessary measures to reduce the development of lymphedema by considering the total number of lymph nodes removed in the dissection material and the number of

metastatic lymph nodes. There are limitations within the scope of our study. First of all, the small number of cases constituted a limitation in our study. In addition, limb diameter measurements were used to evaluate the development of lymphedema in the patients, and volume change measurement was not applied, but the study by Taylor et al. showed that limb diameter measurements appropriate to anatomical points have high reliability (14). In addition, evaluating the quality of life of the patients could have helped us to better consider the clinical lymphedema complaints of the patients.

CONCLUSION

According to the results obtained from our data, there is a correlation between the total number of removed lymph nodes and metastatic lymph nodes and limb diameter differences. It may be beneficial to determine cut-off values for the total number of removed lymph nodes and the number of metastatic lymph nodes and to predict the development of lymphedema in a larger case series. Thus, it may be possible to predict the development of lymphedema, evaluate the results, establish appropriate communication with patients, and detail a personalized treatment.

Ethics Committee Approval: The study has ethical approval from the Istanbul University (Date: 17.03.2023, No: 06).

Informed Consent: All data was anonymized, and the informed consent for every patient was recorded

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