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# Evaluation of skin barrier functions in patients with breast cancer-related lymphedema: Measurement of stratum corneum hydration, sebum level, and transepidermal water loss

## *Meme kanseri ilişkili lenfödemi olan hastalarda deri bariyer fonksiyonlarının incelenmesi: Stratum korneum hidrasyonu, sebum ve transepidermal su kaybının ölçülmesi*

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### Abstract

**Background and Design:** Skin barrier function in patients with breast cancer-related lymphedema (BCRL) has rarely been evaluated. This study aimed to investigate transepidermal water loss (TEWL), stratum corneum hydration (SCH), and sebum level (SL) on the skin of the lymphedema arm in comparison to the skin of the healthy contralateral arm in BCRL patients.
**Materials and Methods:** This cross-sectional study included 40 female patients with unilateral BCRL. TEWL, SCH, and SL were measured using Tewameter®, Corneometer®, and Sebumeter®, respectively. Measurements were taken in each patient's lymphedema arms and healthy contralateral arm. The volar/dorsal regions of the forearm and the dorsal region of the upper arm were determined as measurement sites.
**Results:** In all three measurement areas, there was no significant difference in SCH or SL between the skin of the lymphedema arm and the skin of the healthy contralateral arm. TEWL was significantly higher on the skin of the lymphedema arm than on the healthy arm for the volar forearm regions (p=0.007). However, there was no significant difference in TEWL between the skin of the lymphedema arm and the skin of the healthy contralateral arm in the dorsal forearm or dorsal upper arm region.
**Conclusion:** This study showed that there was no difference in skin barrier functions in the lymphedema arm compared with the healthy contralateral arm, except for higher TEWL in the skin of the volar forearm region of the lymphedema arm in BCRL patients. The detection of changes in skin barrier function in BCRL patients may help in the regulation of optimal skin care of these patients' lymphedema arms.
**Keywords:** Breast cancer-related lymphedema, lymphedema, sebum, transepidermal water loss

### Öz

**Amaç:** Meme kanseri ilişkili lenfödemi (MKİL) olan hastalarda derinin bariyer fonksiyonlarını inceleyen çalışmalar sınırlıdır. Bu çalışmada, MKİL'li hastalarda sağlıklı üst ekstremite ile lenfödemli üst ekstremitenin transepidermal su kaybı (TESK), stratum korneum hidrasyonu (SKH) ve sebum (S) değerlerinin incelenmesi amaçlandı.
**Gereç ve Yöntem:** Bu kesitsel çalışmaya unilateral MKİL'li 40 kadın hasta dahil edildi. TESK, SKH ve S değerleri sırasıyla Tewameter®, Corneometer®, ve Sebumeter® cihazları kullanılarak ölçüldü. Her hastada lenfödem olan kolda ve sağlıklı karşı kolda ölçümler yapıldı. Ön kolun volar/dorsal yüzleri ve üst kolun dorsal yüzü ölçüm bölgeleri olarak belirlendi.

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**Bulgular:** Lenfödemli kol derisi ile sağlıklı kontralateral kol derisinin 3 ölçüm alanında da SKH veya S değerleri açısından istatistiksel olarak anlamlı fark yoktu. TESK, ön kolun volar bölgesinde, sağlıklı kola kıyasla lenfödemli kol tarafında anlamlı olarak daha yüksekti (p=0,007). Ancak, ön kolun dorsal bölgesinde veya üst kolun dorsal bölgesinde lenfödem kolunun derisi ile sağlıklı kontralateral kolun derisi arasında TESK açısından istatistiksel olarak anlamlı fark bulunmadı.
**Sonuç:** MKİL hastalarında, lenfödemli kolun ön kol volar yüzeyinde daha yüksek TESK tespit edildi. MKİL hastalarında, deri bariyer fonksiyonundaki değişikliklerin bilinmesi, bu hastaların lenfödemli kollarının deri bakımını optimal şekilde düzenlemesine yardımcı olabilir.
**Anahtar Kelimeler:** Meme kanseri ilişkili lenfödem, lenfödem, sebum, transepidermal su kaybı

## Introduction

Breast cancer is the most prevalent malignancy in women worldwide[1]. Lymphedema is one of the most common causes of morbidity associated with breast cancer treatment. Despite recent advances in breast cancer treatment, breast cancer-related lymphedema (BCRL) is a common problem that causes severe physical and psychological discomfort[2]. One of the main treatments recommended for managing lymphedema is complex decongestive therapy (CDT). Skin care is one of the components of CDT[3,4].

The limb with lymphedema is prone to soft tissue infection. Cellulitis is the most common soft tissue infection in patients with lymphedema, and recurrent cellulitis episodes worsen lymphedema. Optimal skin care in the upper extremity with lymphedema can provide an important defense against infections, preventing secondary morbidities, such as ulcerations and cellulitis. Skin care and appropriate skin moisturizers can heal cracks[5,6].

Understanding the skin barrier function of patients with BCRL may contribute to regulating appropriate skin care. Unfortunately, there have been few studies on the skin barrier function in patients with lymphedema, where skin care is critical. Therefore, in patients with unilateral BCRL, we aimed to investigate stratum corneum hydration (SCH), sebum level (SL), and transepidermal water loss (TEWL) in the skin of lymphedema arm in comparison with the skin of the healthy contralateral arm.

## Materials and Methods

### Study design and population

This study was approved by Non-interventional Clinical Research Ethics Committee Aydın Adnan Menderes University Faculty of Medicine (approval number: 2020/18, date: 23.01.2020).

In the study, female patients with unilateral BCRL were followed at the Physical Medicine and Rehabilitation Outpatient Clinic of Aydın Adnan Menderes University Hospital in Turkey. Forty female patients with unilateral BCRL were recruited in the study from August 2020 and December 2021. All of the patients provided written informed consent. Lymphedema was graded according to lymphedema staging of the International Society of Lymphology. Stage 1 lymphedema is characterized by an early accumulation of fluid that subsides with limb elevation and pitting may occur. In stage 2 lymphedema, limb elevation alone rarely reduces tissue swelling and pitting manifests. Later in stage 2, pitting in the limb may not be observed. Stage 3 encompasses lymphostatic elephantiasis, where pitting is absent and trophic skin changes have developed[3].

TThe patients in the study did not use topical agents such as moisturizer and sunscreen on their arms until the last one day before the measurements, and did not wear elastic arm garments on the day of the measurements. None of the patients had dermatological conditions in the measurement areas, such as cellulitis, impetigo, and impaired skin integrity.

### Stratum corneum hydration, sebum level, and transepidermal water loss measurements

The measurements were taken in an identical room with certain conditions: a temperature of 20-24 °C and an air humidity of 40-60%. SCH, SL, and TEWL were measured by the same dermatologist using Corneometer® CM825, Sebumeter® SM 815, and Tewameter TM 300® instruments, respectively, coupled to the Multi-Probe-Adapter-5 device (Courage et Khazaka electronic GmbH, Köln, Germany). The capacitance method is used in the Corneometer® CM 825, an instrument for measuring the hydration condition of the stratum corneum[7]. Sebumeter SM 815 uses the translucency of a specific tape that turns transparent after contact with sebum on the skin. The light permeability of the particular tape changes after 30 seconds of skin contact, depending on the amount of sebum in the skin[8]. The measurement of TEWL using Tewameter TM 300® is in $g/m^2/h$ and is based on diffusion in an open chamber[9].

Measurements were taken in the patient's lymphedema arm and healthy contralateral arm. The healthy contralateral arm was used as the control. Before starting the measurements, participants were given sufficient time (at least 15 min) to adapt to the environmental conditions. The measurement areas were not covered with clothing during the waiting period. The mid-volar/dorsal regions of both forearms and the mid-dorsal regions of both upper arms were measured.

TEWL was measured continuously for 30 seconds at each measurement site, and the measurements were averaged. For SCH, three measurements were taken at each site, and the average of the three measurements was used for analysis. Measurements for SL were taken once at each measurement site. All measurements were performed by the same dermatologist.

In addition, upper extremity cutaneous examinations were conducted by the same dermatologist. Mycological examinations were performed as needed. Sociodemographic data and anthropometric measurements of the patients were obtained.

### Statistical Analysis

SPSS software (version 18.0) was used for statistical analysis. The data were analyzed using descriptive analysis, Wilcoxon signed-rank test, and paired sample t-test. The Kolmogorov-Smirnov test was used for the normal data distribution test. The TEWL and SL variables failed the normality test; therefore, the median (25-75%) was used for non-parametric descriptive statistics. For the intragroup comparison, the Wilcoxon signed-rank test was used. SCH variables passed the normality test; thus, mean ± standard deviation was presented for parametric descriptive statistics. For the intragroup comparison, the paired sample t-test was used. $P<0.05$ was accepted as statistically significant in data analysis.

## Results

All 40 patients with BCRL completed the study. The mean age of the patients was 57.2 yr (range: 38-77). Of the 40 patients, 7 (17.5%) had stage 1 lymphedema, 31 (77.5%) had stage 2 lymphedema, and 2 (5.0%) had stage 3 lymphedema. The characteristics of patients with BCRL are shown in Table 1.

There was no significant difference in SCH or SL in all three measurement areas between the lymphedema skin and the control. TEWL was significantly higher in lymphedema for mid-volar forearm regions than in control. However, there was no statistically significant difference in TEWL between the lymphedema and control groups in the mid-dorsal forearm or mid-dorsal upper arm regions (Table 2).

None of the patients had skin infections, such as cellulitis, on their arms. However, a white, macerated tissue surrounded by erythema was observed between the fingers of the lymphedema arm in two patients (Figure 1, 2). A potassium hydroxide examination confirmed Candida; an erosio interdigitalis blastomycetica (EIB) was diagnosed. Both patients had stage 3 lymphedema.

**Table 1. Characteristics of the female patients with breast cancer-related lymphedema (n=40)**

| | |
|---|---|
| **Affected arm** | |
| Right-sided lymphedema | 17 (42.5%) |
| Left-sided lymphedema | 23 (57.5%) |
| **Dominant hand** | |
| Right-handed | 38 (95%) |
| Left-handed | 2 (5%) |
| **Lymphedema stage** | |
| Stage 1 | 7 (17.5%) |
| Stage 2 | 31 (77.5%) |
| Stage 3 | 2 (5.0%) |
| Mastectomy | 40 (100.0%) |
| Axillary surgery | 40 (100.0%) |
| Radiotherapy | 38 (95.0%) |
| Duration of lymphedema (months) | 49 (1-192) |

Data were shown as numbers (%).

## Discussion

TEWL is an important factor for assessing the integrity of the skin barrier. Higher TEWL implies skin barrier dysfunction, whereas lower TEWL indicates a recovered or undamaged skin barrier[10]. Ferguson et al.[11] found that TEWL in podoconiosis, a common cause of lymphedema in barefoot workers, was not different from controls. Yu et al.[12] demonstrated that in 90 patients with unilateral chronic lymphedema of extremities (34 with upper extremity, 56 with lower extremity), the values of TEWL were significantly increased in lymphedema skin when compared with controls. Our study found that TEWL values

**Figure 1.** White, macerated tissue surrounded by erythema between the fingers of the lymphedema arm (patient 1)

**Figure 2.** White, macerated tissue surrounded by erythema between the fingers of the lymphedema arm (patient 2)

**Table 2. Skin barrier functions of the lymphedema arm and healthy contralateral arm**

| | Lymphedematous arm | Healthy contralateral arm | p |
|---|---|---|---|
| SCH (volar forearm)[a] | 45.13±13.72 | 45.74±12.37 | 0.575 |
| SCH (dorsal forearm)[a] | 41.70±16.08 | 42.56±14.70 | 0.543 |
| SCH (dorsal of upperarm)[a] | 41.10±12.76 | 41.31±11.51 | 0.870 |
| SL (volar forearm)[b] | 0 (0-0) | 0 (0-0) | 0.299 |
| SL (dorsal forearm)[b] | 0 (0-2.00) | 0 (0-1.75) | 0.761 |
| SL (dorsal of upperarm)[b] | 0 (0-1.00) | 0 (0-1.75) | 0.699 |
| TEWL (volar forearm)[b] | 10.95 (6.75-20.90) | 10.10 (6.35-14.15) | 0.007* |
| TEWL (dorsal forearm)[b] | 9.80 (6.32-18.90) | 10.00 (6.95-15.87) | 0.747 |
| TEWL (dorsal of upperarm)[b] | 8.90 (5.45-17.62) | 9.05 (6.32-13.70) | 0.707 |

SCH: Stratum corneum hydration, SL: Sebum level, TEWL: Transepidermal water loss. [a]Data were shown as mean ± standard deviation. Paired sample t-test was used to analyze the data. [b]Data were shown as median ($25^{th}$-$75^{th}$). Wilcoxon signed-rank test was used to analyze the data. *Statistically significant level ($p<0.05$)

were higher in the lymphedema skin but only in the mid-volar forearm region. TEWL is influenced by person-related factors (age, sex, race, anatomical sites, skin surface temperature, sweating, skin damage, and skin diseases) and environmental and instrumental variables[13]. More studies are needed to understand why TEWL increases in the volar forearm with lymphedema. Furthermore, several studies have shown that skin care decreases TEWL of lymphedema extremities[14-16]. In light of this information, skin care in lymphedema extremities, particularly the volar forearm, should not be neglected.

Killaars et al.[17] found no significant difference in SCH levels between lymphedema skin and healthy arms in patients with BCRL. In line with this study, no significant difference in SCH was found between lymphedema and control in all of the three measurement areas in our study. Lymphedema is a localized tissue swelling caused by extreme retention of lymphatic fluid in the interstitial compartment induced by damaged lymphatic drainage[18]. Many studies have shown that tissue fluid in lymphedema patients is higher in lymphedema limbs than in control limbs using various methods[12,19]. However, Corneometer® specifically assesses SCH. Therefore, we may conclude that the local fluid increase in lymphedema did not affect SCH.

To the best of our knowledge, SL has not been previously measured in patients with BCRL. We found no significant difference in SL between the lymphedema and the control groups in all three measurement regions. The arm has a sebum-poor region compared with the face[9,20]. The low SL in our study is possibly related to the fact that the arm is poor in sebum.

In our study, EIB was found between the fingers of the lymphedema hands of two patients with stage 3 lymphedema. EIB is a cutaneous infection caused by Candida, an intertrigo affecting the interdigital webs, most often the third and fourth interdigital webs[21]. Two patients with stage 3 lymphedema showed more prominent skin folds and decreased interdigital spaces between their fingers of the lymphedema hand. Intertrigo is most likely facilitated by increased lymphedema-related skin folds and reduced lymphedema-related interdigital spaces. The literature found that toe web intertrigo is one of the major risks for developing leg erysipelas[22,23]. Early diagnosis and treatment of intertrigo in patients with BCRL are important to prevent the development of soft tissue infections known to worsen lymphedema. Therefore, patients with BCRL and the physicians following these patients should be informed about intertrigo.

### Study Limitations

The changes in skin barrier functions could not be evaluated according to the lymphedema stage due to fewer patients with stage 1 and stage 3 lymphedema. Studies with larger population groups that include patients at all three stages may provide more valuable information.

## Conclusion

This study showed no difference in skin barrier functions in lymphedema skin compared with the control, except for higher TEWL in the skin of the volar forearm region of the lymphedema arm in patients with BCRL. Detecting changes in skin barrier function in patients with BCRL may help regulate optimal skin care of these patients' lymphedema arms.

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### Ethics

**Ethics Committee Approval:** This study was approved by Non-interventional Clinical Research Ethics Committee Aydın Adnan Menderes University Faculty of Medicine (approval number: 2020/18, date: 23.01.2020).

**Informed Consent:** Written informed consent forms were obtained from all the participants.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: M.G., E.T., Concept: M.G., Design: M.G., E.T., M.U., E.Ş., N.Ş., Data Collection or Processing: M.G., Analysis or Interpretation: M.G., E.T., M.U., Literature Search: M.G., Writing: M.G.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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