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Original Article

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# Skin Barrier Function Assessment: Electrical Impedance Spectroscopy Is Less Influenced by Daily Routine Activities Than Transepidermal Water Loss

**Lisa Huygen** [1,2], **Pauline Marie Thys** [1], **Andreas Wollenberg** [2,3,4], **Jan Gutermuth** [1,2], **Inge Kortekaas Krohn** [1,2]

[1]Vrije Universiteit Brussel (VUB), Skin Immunology & Immune Tolerance (SKIN) Research Group, Brussels, Belgium
[2]Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Department of Dermatology, Brussels, Belgium
[3]Department of Dermatology and Allergy, Ludwig-Maximilian-University, Munich, Germany
[4]Department of Dermatology and Allergy, University Hospital Augsburg, Augsburg, Germany

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**Corresponding Author:**
**Lisa Huygen**
Vrije Universiteit Brussel (VUB), Skin Immunology & Immune Tolerance (SKIN) Research Group, Laarbeeklaan 103, 1090, Brussels, Belgium.
Email: lisa.huygen@vub.be



## ABSTRACT

**Background:** Skin barrier function assessment is commonly done by measuring transepidermal water loss (TEWL). An important limitation of this method is the influence of intrinsic and extrinsic factors. Electrical impedance spectroscopy (EIS) is a lesser-established method for skin barrier function assessment. Some influential factors have been described, but no guidelines exist regarding the standardization of these measurements.
**Objective:** To evaluate the effect size of daily routine activities on TEWL and EIS, as well as their correlation with age and anatomical differences.
**Methods:** Healthy participants (n=31) were stratified into three age groups (18–29, 30–49, and ≥50 years). In a climate-controlled room, EIS and TEWL measurements were performed on the left and right volar forearm and abdomen.
**Results:** Body cream application decreased TEWL and EIS values after 15 and 90 minutes. Skin washing decreased TEWL for 15 minutes and EIS values for at least 90 minutes. TEWL was increased 5 minutes after moderate to intense exercise. Coffee intake increased TEWL on the abdomen after 60 minutes. TEWL and EIS values did not correlate with participants' age and no anatomical differences were observed. No correlation was observed between TEWL and EIS.
**Conclusion:** Body cream application and skin washing should be avoided at least 90 minutes prior to measurements of TEWL and EIS. Exercise and coffee intake should also be avoided prior to TEWL measurements. EIS may be a promising tool for skin barrier function assessment as it is less affected by daily routine activities than TEWL.

**Keywords:** Activities of Daily Living; Electric Impedance; Hydration; Skin Barrier; Transepidermal water loss; Washing

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## INTRODUCTION

An intact epidermal barrier protects against pathogen invasion, withstands chemical and physical assault, and controls physiological loss of water and solutes through the skin[1-4]. The stratum corneum (SC) contributes significantly to this barrier function[5]. The SC consists of flattened, anucleate corneocytes, which are interconnected by desmosomes and surrounded by lamellar lipid sheets. These are composed of ceramides, cholesterol, and free fatty acids, which form a hydrophobic matrix[3,6,7]. Epidermal tight junctions, adherence junctions, and desmosomes also contribute to the skin barrier function[3,8].

Epidermal barrier disruption contributes to the pathogenesis of skin diseases like contact dermatitis, ichthyosis, and atopic dermatitis (AD)[2,7,9-11]. Skin barrier function assessment is important to evaluate skin health and the extent of skin diseases. Skin examination already provides clinically relevant information. However, measurements of biophysical skin properties are needed for the scientific assessment of this barrier function. The most frequently used method is the measurement of transepidermal water loss (TEWL). It is defined as the water amount diffusing across a fixed skin area per time unit[12]. TEWL reflects the inside-out perspective of the skin barrier and skin permeability formed by the SC thickness and compactness, SC lipid layers, and tight junction integrity[3,12,13]. Skin barrier disruption increases permeability and TEWL[14].

Electrical impedance spectroscopy (EIS), a lesser-established method, measures the response of a skin region to a low-voltage electrical alternating current at various frequencies[15,16]. EIS is a single value parameter, which is influenced by skin hydration, SC thickness, condition of water channels, and cell properties (size, shape, orientation, compactness, and structure of the cell membrane) at the same time[17-19]. A magnitude index (MIX) value can be calculated from EIS results, which is used for assessment of skin barrier function[20,21]. This value is the ratio of the total skin impedance magnitude at two fixed frequencies of 20 kHz and 500 kHz ($MIX = |Z_{20\,kHz}|/|Z_{500\,kHz}|$)[22].

Multiple extrinsic and intrinsic factors can influence skin barrier function measurements[12,18,23-33]. The influence of aging on the skin barrier remains controversial, whereas some studies observed decreased skin barrier function, which resulted in increased MIX values and decreased TEWL[18,33-36]. Differences in sweat gland activity, SC thickness, and skin hydration cause disparities in TEWL and EIS at different anatomical locations[28,33]. Extended water exposure leads to disruption of intercellular lipid lamellae, and corneocyte swelling, which results in increased TEWL and skin impedance[29,30,37,38]. Strenuous efforts trigger arteriolar vasodilatation, increase capillary blood flow, and stimulate sweat glands, leading to increased SC capacitance and TEWL[32,39] Finally, body cream/lotion application causes skin hydration, skin barrier improvement, and protection against water loss and pathogen invasion resulting in decreased TEWL and MIX values[22,38,40]. The effects of the above-mentioned influencing factors were mainly studied in well-controlled, and sometimes artificial settings.

The European Expert Group on Efficacy Measurement of Cosmetics and Other Topical Products (EEMCO) developed guidelines for TEWL assessment to standardize measurement results in clinical study contexts[15,23]. An acclimatization period of 15–30 minutes in a room with a temperature of 20–22°C and relative humidity of 40–60% is advised. Eating, perspiration, water exposure, usage of skin products, and smoking before and during measurements should be avoided[15,23]. Caffeine intake is also discouraged by current recommendations, but its effect on TEWL has not yet been studied. This extensive list of restrictions can prevent potential subjects from participating in a study.

Because many situations were initially examined in artificial settings, this study aimed to analyze the effect of relevant daily routine activities on TEWL measurements and EIS. Moreover, no guidelines exist regarding the standardization of EIS for skin barrier function assessment. We hypothesized that body cream application, skin washing, physical activity, and coffee intake are relevant daily activities that might affect these measurements. Additionally, the correlation between TEWL and MIX values with participants' age and the presence of anatomical differences was examined.

## MATERIALS AND METHODS

### Study participants

The study was approved by the local Committee of Medical Ethics of the Universitair Ziekenhuis Brussel (EC-2021-303). Ethical principles were performed according to the Declaration of Helsinki, Good Clinical Practice, and national Belgian law. All participants were informed about the study content. Eligible Dutch- or French-speaking subjects were enrolled if ≥18 years after giving written informed consent. 31 non-smoking healthy participants without known skin diseases were included from October 2021 until December 2021 at the Department of Dermatology, Vrije Universiteit Brussel/Universitair Ziekenhuis Brussel. Participants were stratified into three age groups, 18–29 (n=11), 30–49 (n=10), and ≥50 years old (n=10).

### Study design

Participants had to refrain from applying skin products, washing their volar forearm and abdomen, making strenuous efforts, and drinking hot and/or caffeine/theine-containing beverages for at least 1 hour prior to their visit. Measurements took place after an

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acclimatization period of 30 minutes in a standardized relative humidity-controlled room (humidity of 50–55%, temperature of 22°C, and a roller blind to avoid direct sun exposure) thereby eliminating possible environmental influences.

Measurements were performed within two visits. Baseline TEWL and MIX values were obtained on the volar forearm and abdomen at each visit. At visit one, TEWL measurements and EIS were performed 15 and 90 minutes after the application of 1/4 fingertip unit (FTU) of water in oil emulsion Emollient Cream (Dexeryl®; Pierre Fabre Dermatologie, Paris, France) containing glycerin and petrolatum on the right volar forearm and abdomen (area: ±ere100 cm$^2$). Next, the left forearm and abdomen were washed with tepid water (temperature of 36–38°C) and ½ FTU of shower cream containing glycerin and sweet almond oil (Pure Care Shower Cream, Creme Soft, Nivea®; Nivea, Hamburg, Germany) for one minute. Measurements took place after 15 and 90 minutes. On the second visit, participants had to walk for 5 minutes at low intensity in the corridor (climate provided by central ventilation system), after which measurements were performed at 5, 30, and 60 minutes. Next, TEWL measurements and EIS were performed 5, 30, and 60 minutes after walking up and down stairs for 5 minutes (moderate to high intensity). Finally, measurements were performed 5, 20, and 60 minutes after finishing a cup of coffee (Douwe Egberts Lungo 6 Dessert).

### Transepidermal water loss

The Multi Skin Test Center MC 1000 (Courage+Khazaka electronic GmbH, Köln, Germany) and Complete Skin Investigation (CSI) software were used for assessing TEWL[41]. This device generates a TEWL index score (1-20) using an open-chamber probe with two sensors which is placed on the participant's skin[12,15,41,42]. An increasing score corresponds to an increasing TEWL, which reflects a skin barrier deterioration. Three reproducible measurements, each taking 15 seconds to complete, were used to calculate a final average score.

### Electrical impedance spectroscopy

EIS was performed with the Nevisense device (SciBase AB, Stockholm, Sweden)[43]. Skin impedance is measured at 35 different frequencies, logarithmically distributed from 1 kHz to 2.5 MHz, at four different depths, and 10 different permutations. The applied voltage and resulting current are limited to 150 mV and 75 μA[19]. This device uses a spring-loaded probe with a disposable gold-plated electrode consisting of small micro-invasive pins[19]. Each measurement, taking approximately 10 seconds to complete, was preceded by soaking the test site with 0.9% saline solution (wound cleansing wipe, Salvequick®; Orkla Wound Care, Barcelona, Spain) for approximately 30 seconds to reduce the naturally high impedance of the stratum corneum and to obtain a good electrical connection between the probe and the skin[19,44]. Apart from mild erythema, measurements did not cause harm or discomfort for participants[19].

The Nevisense device generates a MIX value for skin barrier function assessment. This value is defined as the ratio of total skin impedance magnitude at two fixed frequencies of 20 kHz and 500 kHz ($\text{MIX}=|Z_{20\ \text{kHz}}|/|Z_{500\ \text{kHz}}|$)[22]. Impedance measurements at 20 kHz are confined to the extracellular space of the stratum corneum, while the impedance measured at 500 kHz reflects both intra- and extracellular properties and capacitive properties of cell membranes of deeper skin layers[19,33,44]. The final MIX value was calculated by the average of two reproducible measurements.

### Statistical analysis

Statistical analyses were performed using SPSS Statistics version 28 (IBM Corp., Armonk, NY, USA) and GraphPad Prism 9 (GraphPad Software Inc., San Diego, CA, USA). The normality of distribution of data sets was determined using Kolmogorov-Smirnov test. A one-way Repeated-Measures analysis of variance or Friedman test was performed to evaluate the influence of daily routine activities on TEWL measurements and EIS. A simple linear regression (Pearson's correlation coefficient) or Spearman correlation was performed to assess the correlation between age and TEWL and MIX values and between TEWL and MIX values. Lastly, TEWL and MIX values at different anatomical locations were compared by a Friedman test.

## RESULTS

In total, 31 healthy participants (13 men [41.9%], 18 women [58.1%]) with a median age of 36 years old (interquartile range: 24.0–56.0) were included in this study. Of those, 26 had a Fitzpatrick skin phototype of 2, four of them had type 3, and one had type 4 (**Supplementary Table 1**).

### Body cream application and skin washing decreased TEWL and MIX values, while exercise and coffee intake increased TEWL

Body cream application decreased TEWL on the volar forearm (15 min: $p<0.0001$; 90 min: $p=0.0077$) and abdomen (15 min: $p<0.0001$; 90 min: $p=0.0133$) compared to baseline (**Fig. 1A and B**). The MIX value also decreased after body cream application on the forearm (15 min: $p<0.0001$; 90 min: $p=0.0015$) and abdomen (15 min: $p<0.0001$; 90 min: $p<0.0001$) (**Fig. 2A and B**). A lower TEWL was observed 15 minutes after washing the volar forearm ($p<0.0001$) and abdomen ($p=0.0005$) with a shower cream containing glycerin and sweet almond oil. This effect was not present after 90 minutes (**Fig. 1C and D**). Skin washing


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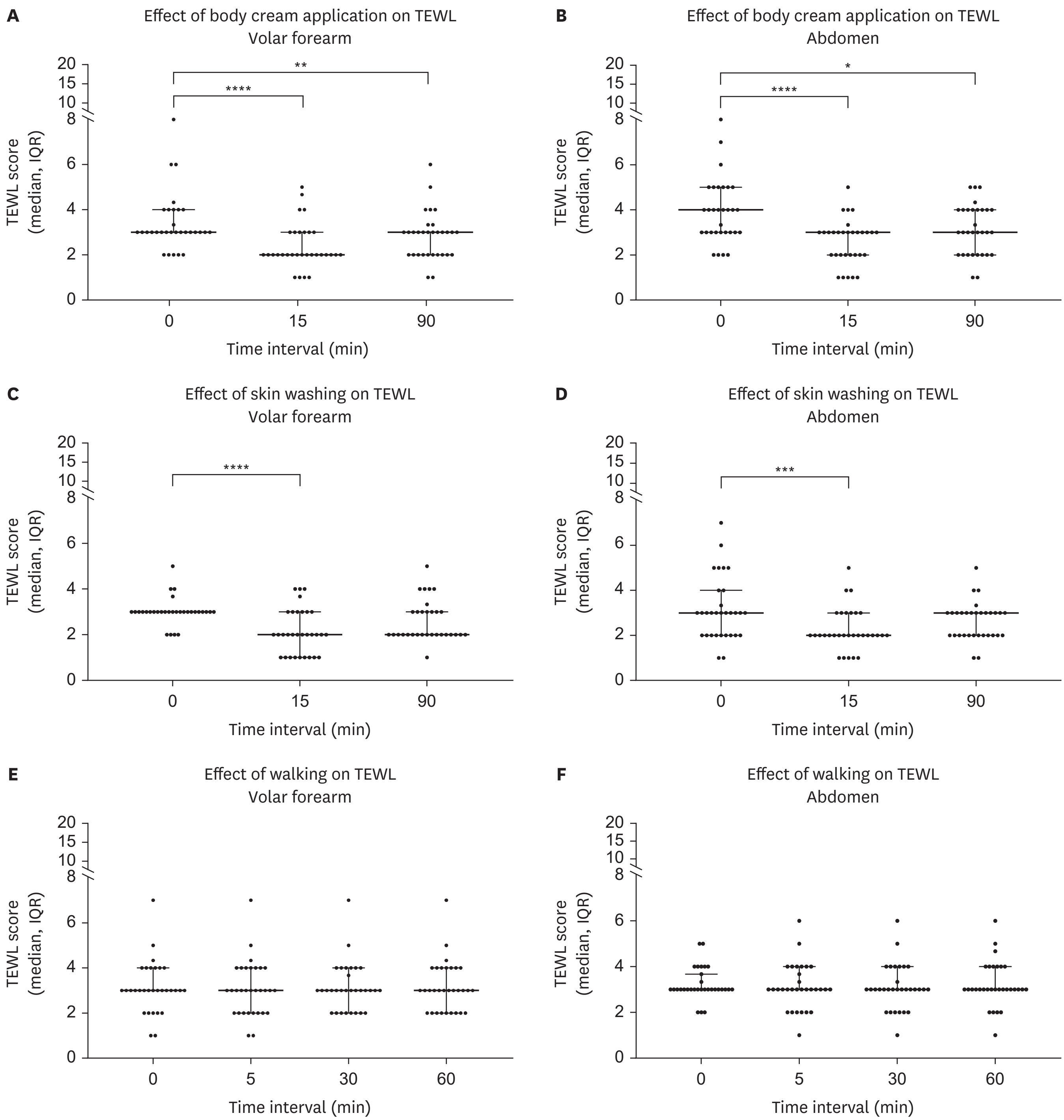


**Fig. 1.** The effect of daily routine activities on results of TEWL measurements on the volar forearm and abdomen. TEWL was measured in healthy subjects (n=31) at baseline and 15 and 90 minutes after body cream application on the volar forearm (A) and abdomen (B). Next, TEWL measurements were performed 15 and 90 minutes after skin washing on the volar forearm (C) and abdomen (D). Five, 30, and 60 minutes after walking the effect of low-intensity effort was measured on the volar forearm (E) and abdomen (F). The effect of moderate to intense effort was measured on the volar forearm (G) and abdomen (H). Five, 30, and 60 minutes after walking up and down stairs. Finally, TEWL was measured 5, 20, and 60 minutes after coffee intake on the volar forearm (I) and abdomen (J). Each individual point represents the mean value of the repeated individual measurements per participant. Data are given as median and interquartile range. A one-way repeated measure ANOVA or nonparametric Friedman test was performed.

TEWL: transepidermal water loss, ANOVA: analysis of variance.

*$p \le 0.05$, **$p \le 0.01$, ***$p \le 0.001$, ****$p \le 0.0001$.

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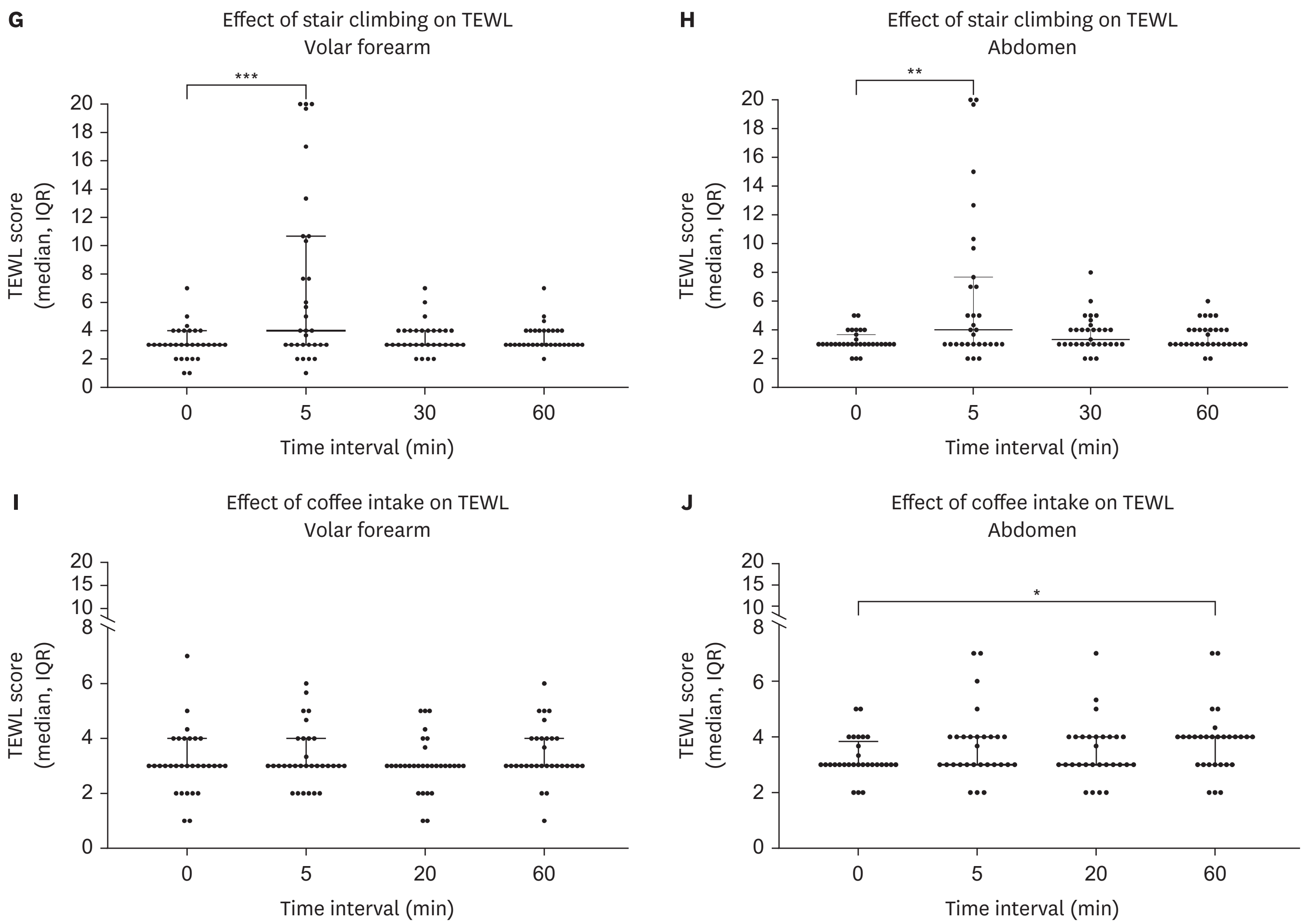


**Fig. 1.** (Continued) The effect of daily routine activities on results of TEWL measurements on the volar forearm and abdomen. TEWL was measured in healthy subjects (n=31) at baseline and 15 and 90 minutes after body cream application on the volar forearm (A) and abdomen (B). Next, TEWL measurements were performed 15 and 90 minutes after skin washing on the volar forearm (C) and abdomen (D). Five, 30, and 60 minutes after walking the effect of low-intensity effort was measured on the volar forearm (E) and abdomen (F). The effect of moderate to intense effort was measured on the volar forearm (G) and abdomen (H). Five, 30, and 60 minutes after walking up and down stairs. Finally, TEWL was measured 5, 20, and 60 minutes after coffee intake on the volar forearm (I) and abdomen (J). Each individual point represents the mean value of the repeated individual measurements per participant. Data are given as median and interquartile range. A one-way repeated measure ANOVA or nonparametric Friedman test was performed.
TEWL: transepidermal water loss, ANOVA: analysis of variance.
*$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$, ****$p \leq 0.0001$.

also decreased the MIX value on forearm (15 min: $p<0.0001$; 90 min: $p<0.0001$) and abdomen (15 min: $p<0.0001$; 90 min: $p<0.0001$) (**Fig. 2C and D**). Walking at low intensity did not influence TEWL measurements and EIS (**Figs. 1E, 1F, 2E, and 2F**). An increased TEWL was observed 5 minutes after moderate to intense exercise (walking up and down stairs) on the forearm ($p=0.0007$) and abdomen ($p=0.0051$). This increase was not significantly detectable after 30 and 60 minutes (**Fig. 1G and H**). EIS was not influenced by moderate to intense exercise (**Fig. 2G and H**). Finally, coffee intake increased TEWL after 60 minutes on the abdomen ($p=0.0146$) (**Fig. 1I and J**), but had no effect on EIS (**Fig. 2I and J**).

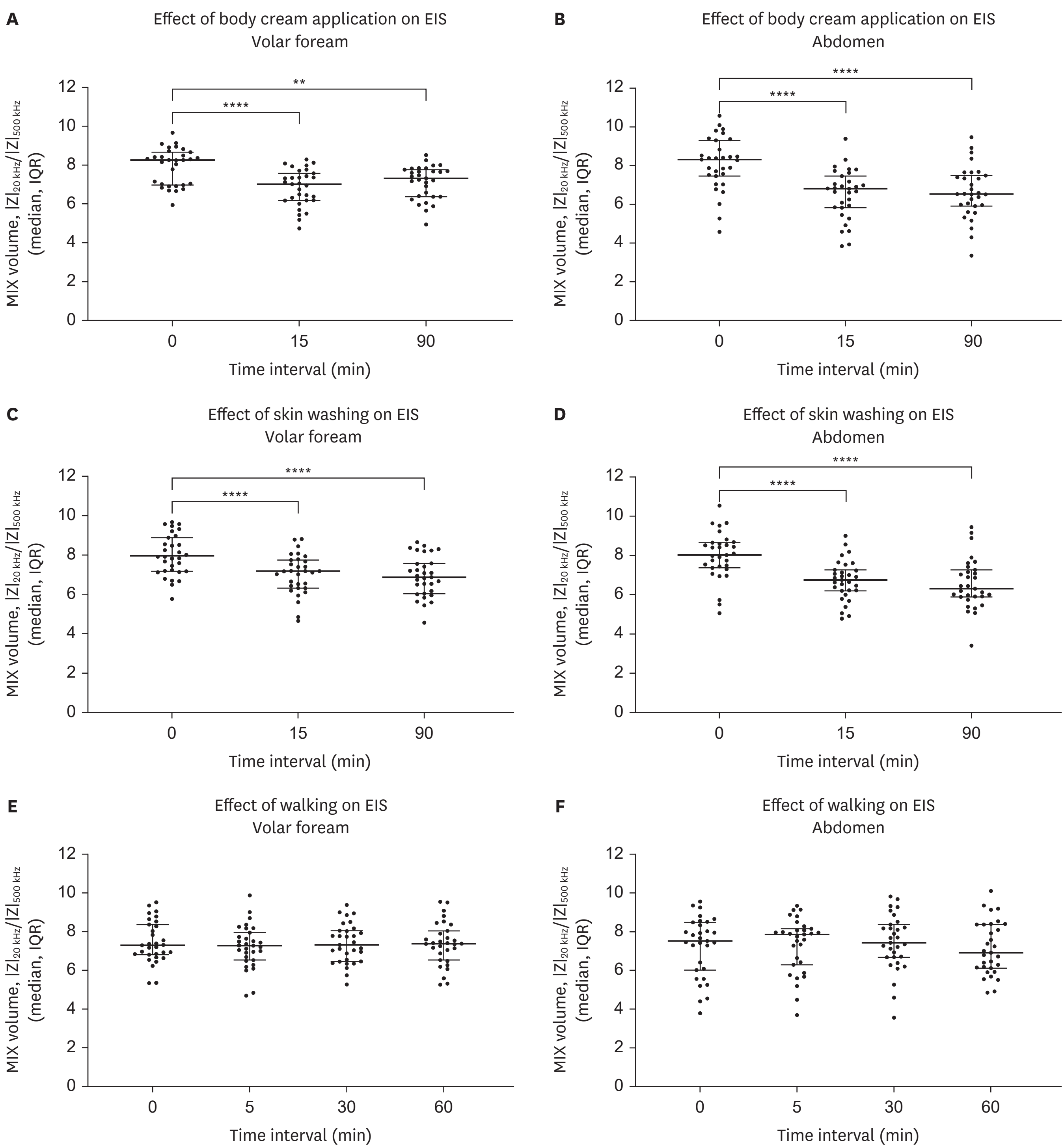


**Fig. 2.** The effect of daily routine activities on results of EIS on the volar forearm and abdomen. MIX values were measured in healthy subjects (n=31) at baseline and 15 and 90 minutes after body cream application on the volar forearm (A) and abdomen (B). Next, EIS was performed 15 and 90 minutes after skin washing on the volar forearm (C) and abdomen (D). Five, 30, and 60 minutes after walking the effect of low-intensity effort was measured on the volar forearm (E) and abdomen (F). The effect of moderate to intense effort was measured on the volar forearm (G) and abdomen (H). Five, 30, and 60 minutes after walking up and down stairs. Finally, MIX values were measured 5, 20, and 60 minutes after coffee intake on the volar forearm (I) and abdomen (J). Each individual point represents the mean value of the repeated individual measurements per participant. Data are given as median and interquartile range. A one-way repeated measure ANOVA or nonparametric Friedman test was performed.
EIS: electrical impedance spectroscopy, ANOVA: analysis of variance.
**$p \le 0.01$, ****$p \le 0.0001$.

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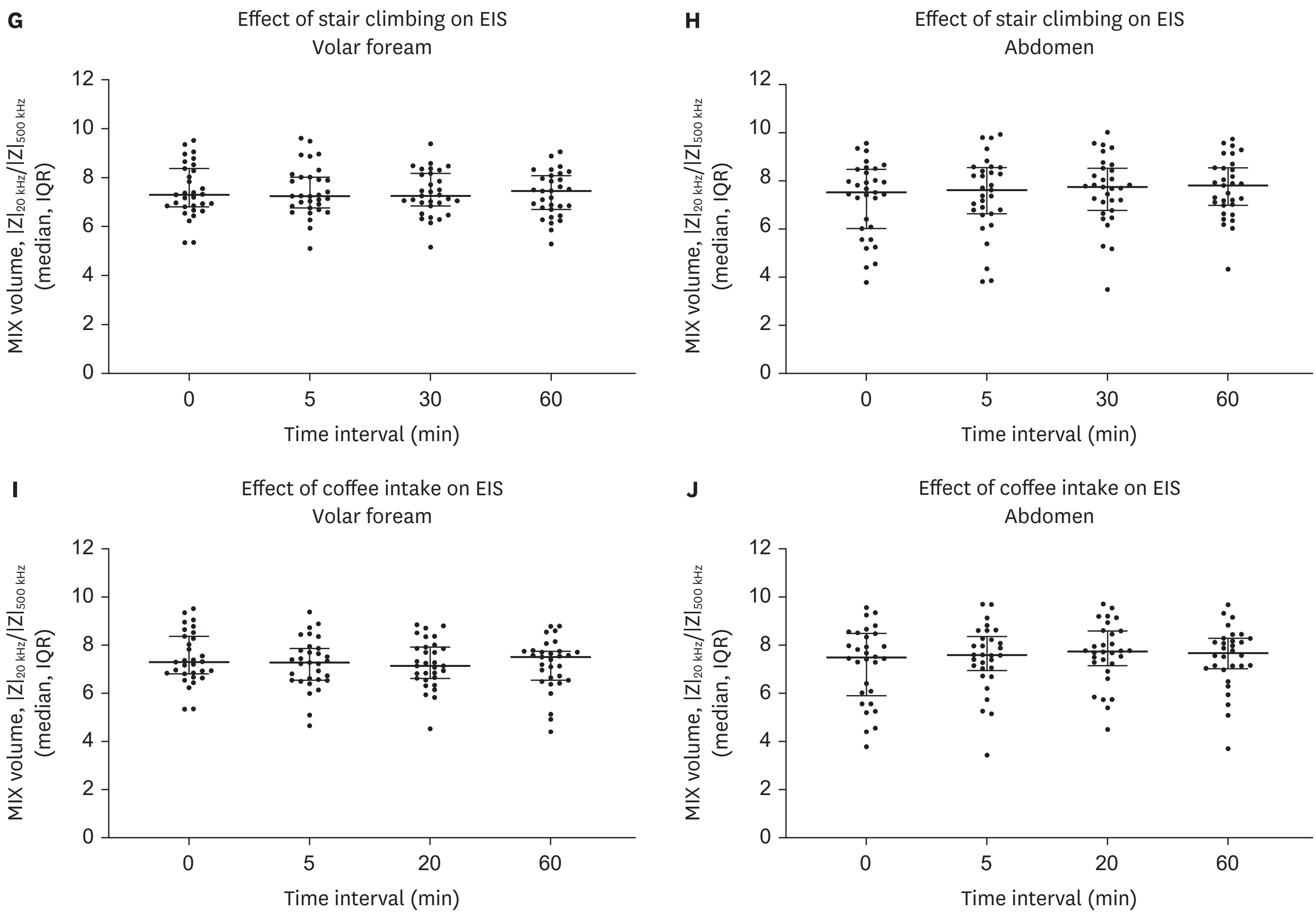


**Fig. 2.** (Continued) The effect of daily routine activities on results of EIS on the volar forearm and abdomen. MIX values were measured in healthy subjects (n=31) at baseline and 15 and 90 minutes after body cream application on the volar forearm (A) and abdomen (B). Next, EIS was performed 15 and 90 minutes after skin washing on the volar forearm (C) and abdomen (D). Five, 30, and 60 minutes after walking the effect of low-intensity effort was measured on the volar forearm (E) and abdomen (F). The effect of moderate to intense effort was measured on the volar forearm (G) and abdomen (H). Five, 30, and 60 minutes after walking up and down stairs. Finally, MIX values were measured 5, 20, and 60 minutes after coffee intake on the volar forearm (I) and abdomen (J). Each individual point represents the mean value of the repeated individual measurements per participant. Data are given as median and interquartile range. A one-way repeated measure ANOVA or nonparametric Friedman test was performed.
EIS: electrical impedance spectroscopy, ANOVA: analysis of variance.
**$p \leq 0.01$, ****$p \leq 0.0001$.

### Age does not correlate with TEWL and MIX values

No correlation was observed between participants' age and TEWL at all anatomical locations. (**Fig. 3**). A non-significant trend toward negative correlation was observed between age and MIX values on all anatomical locations (**Fig. 4**).

### No differences in TEWL and MIX values were observed between volar forearm and abdomen

TEWL and MIX values did not significantly differ when comparing the volar forearm and abdomen on right and left bodyside (**Fig. 5**).

### No correlation exists between TEWL and MIX values

No correlation was observed between TEWL and MIX values (**Fig. 6**).

## DISCUSSION

TEWL measurements and EIS reflect different skin properties. Therefore, these measurement techniques can not readily be compared. TEWL mainly reflects skin permeability by measuring water evaporation[12,14]. This permeability depends on the SC lipid layer and tight junctions of the viable epidermis[3]. A major drawback of TEWL measurements lies in its susceptibility to temperature, humidity, and other factors, which requires a dedicated sheltered space and therefore impedes its widescale use. EIS reflects the extra- and intracellular environment, cell membrane structure, and other skin cell properties like size, shape, orientation, and compactness[17-19]. To gain knowledge on the potential value of EIS for skin barrier function analysis, we


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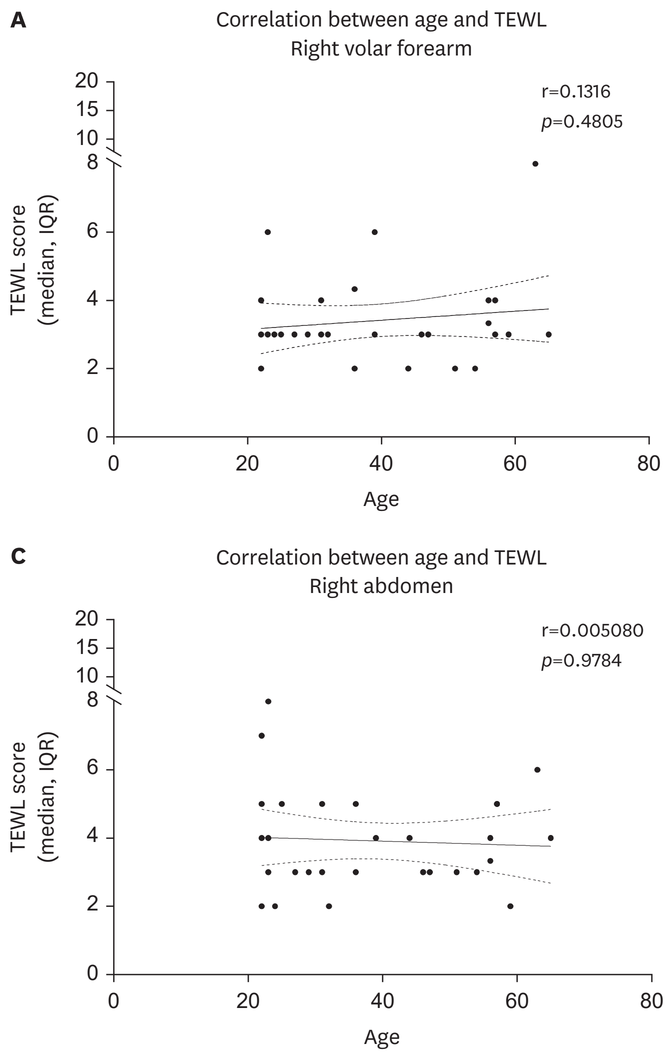


**Fig. 3.** Correlation between participants' age and TEWL. The relationship between age and TEWL was analyzed in healthy individuals (n=31) on the: (A) right volar forearm (B) left volar forearm, (C) right abdomen, and (D) left abdomen. Each individual point represents the mean value of the reproducible measurements per participant. A simple linear regression with the calculation of the Pearson's correlation coefficient or nonparametric Spearman correlation was used. *p*-values of ≤0.05 are considered significant.
TEWL: transepidermal water loss.

compared TEWL measurements and EIS side by side for factors, such as daily routine activities, age, and anatomical location in homeostatic conditions.

Body cream application and skin washing with a shower cream containing glycerin and sweet almond oil reduced TEWL and MIX values in comparable patterns, while exercise and coffee intake increased TEWL measurements, but not MIX values.

TEWL and MIX values were decreased 15 and 90 minutes after body cream application. This could be explained by the hydrating and moisturizing effect of the body cream due to the presence of substances, such as glycerol, white soft paraffin, liquid paraffin, and dimethicone[40,45-47]. Additionally, these substances protect against water loss through the skin, which contributes to a decreased TEWL[40,45,47,48]. Skin hydration decreases skin impedance at all frequencies, most likely due to better current conductivity[22]. Body cream application will mainly lower extracellular resistive properties of superficial skin layers (measured at 20 kHz) by filling pre-existing air-filled voids like hair follicles, sweat glands, and furrows, while intracellular resistive properties and capacitive properties (measured at 500 kHz) are less influenced[22]. The greater influence of body cream application on the impedances measured at 20 kHz results in a decreased MIX value.

Skin washing with tepid water and shower cream for one minute decreased TEWL for 15 minutes and MIX values for 15 and at least 90 minutes on both anatomical locations. Our observation of decreased TEWL is in contrast to previously documented increased TEWL after water exposure, supposedly due to evaporation of remaining water and disruption of SC intercellular lipid

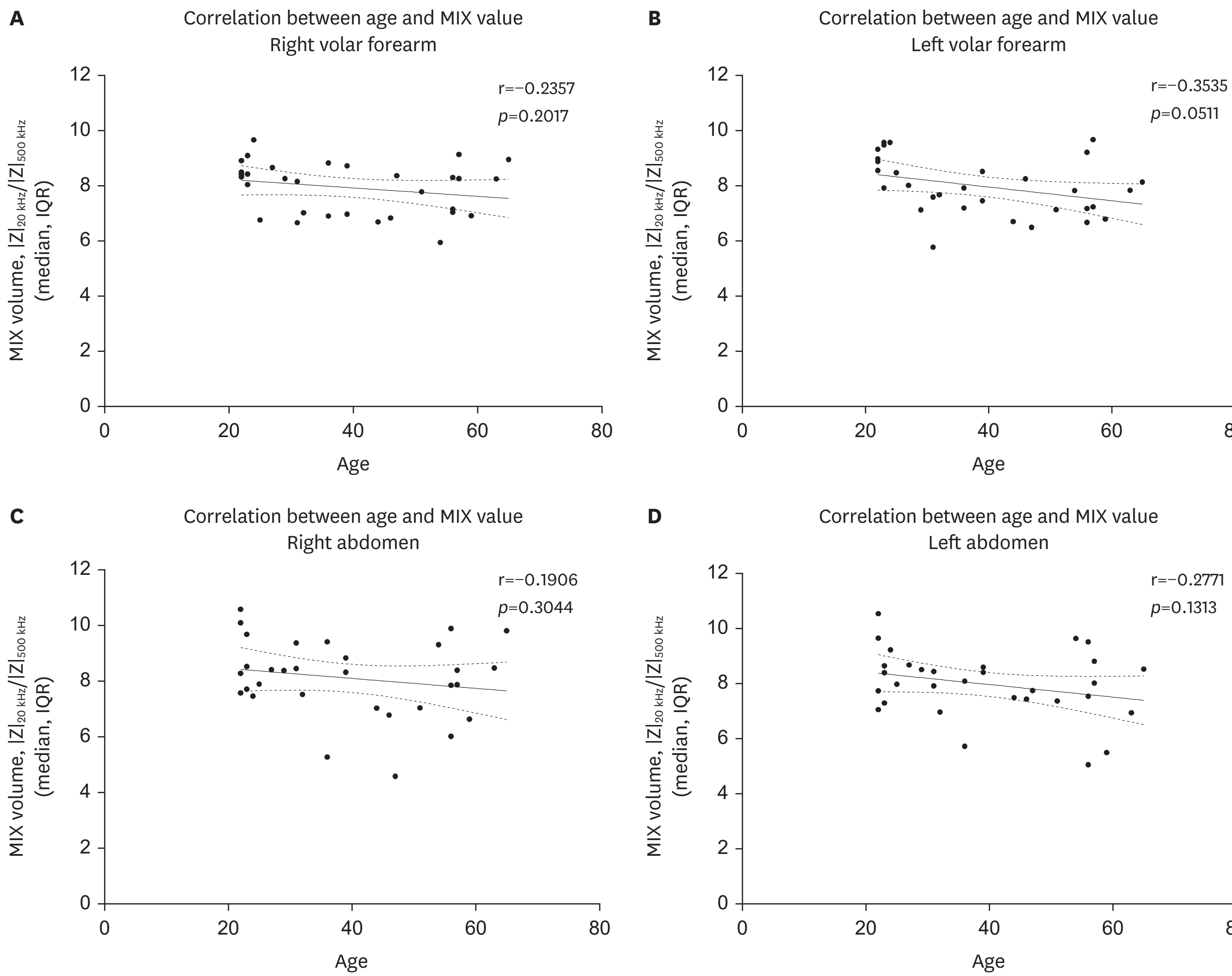


**Fig. 4.** Correlation between participants' age and MIX values. The relationship between age and MIX value was analyzed in healthy individuals (n=31) on the: (A) right volar forearm, (B) left volar forearm, (C) right abdomen, and (D) left abdomen. Each individual point represents the mean value of the reproducible measurements per participant. A simple linear regression with the calculation of the Pearson's correlation coefficient or nonparametric Spearman correlation was used. *p*-values of ≤0.05 are considered significant.
MIX: magnitude index.

layers[29]. These contradictory results may be explained by the limited duration of water exposure (one minute in our study versus 30 minutes for five consecutive days in previous studies) and the hydrating properties of glycerin and sweet almond oil present in the soap used in this study[45]. Decreased MIX values after skin washing may be due to the hydrating properties of glycerin and sweet almond oil present in the soap and the role of water in altering extracellular resistive properties of superficial skin layers by filling pre-existing voids like hair follicles, sweat glands, and furrows[22].

Future studies should address the duration of the above-mentioned effects in order to optimize recommendations about body cream usage and skin washing prior to skin barrier function assessment.

Increased TEWL following exercise was in line with previous reports and might be triggered by vasodilatation, increased blood flow, increased body temperature, and stimulated sweat glands during and directly after exercise[39]. Perspiration will be detected by the TEWL probe together with the true TEWL, resulting in increased TEWL values[32,49]. Since this influence was not observed after 30 and 60 minutes, the acclimatization period currently foreseen in the EEMCO guidelines is sufficient to eliminate influences of activity on TEWL measurements[23]. Physical activity did not influence EIS. This method might be less sensitive to perspiration, due to cleaning and moistening of the test area prior to measurements. The effect of physical activity on EIS has not been studied previously.


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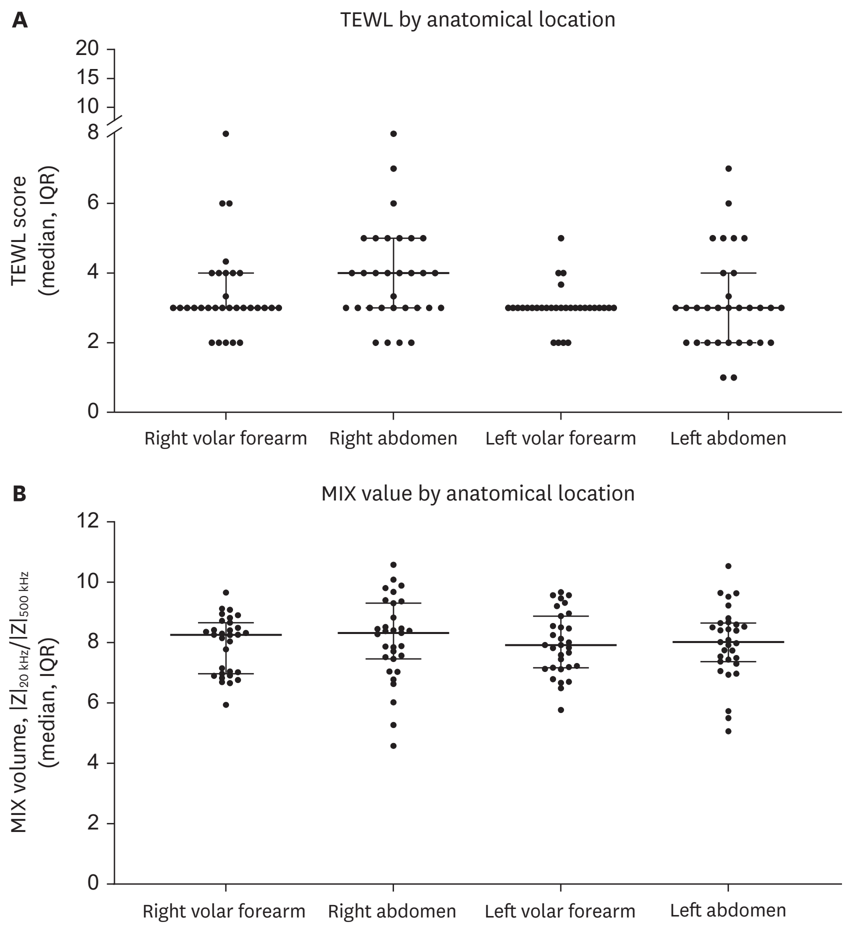


**Fig. 5.** Differences in TEWL and MIX values between the volar forearm and abdomen on the left and right side. (A) Anatomical differences of TEWL. (B) Anatomical differences of MIX values. Each individual point represents the mean value of the reproducible measurements per participant. Baseline data from healthy subjects (n=31) are given as median and interquartile range. A nonparametric Friedman test was performed.
TEWL: transepidermal water loss, MIX: magnitude index.

The effect of coffee intake on TEWL measurements and EIS was not yet investigated. In this study, coffee intake increased TEWL after 60 minutes on the abdomen. This effect may be explained by the high temperature of the drink leading to a slight increase in body temperature resulting in vasodilation and perspiration[50,51]. Additionally, caffeine increases intra-arterial blood pressure and stimulates the sympathetic nervous system, resulting in increased sweat gland activity[50,51]. On the volar forearm, TEWL did not increase after coffee intake. This may be explained by the fact that the evaporation of sweat on the forearm is not hindered by occlusion caused by clothes when compared to the abdomen. Further research is necessary to evaluate whether high temperature, caffeine content, or a combination of both factors are responsible for increased TEWL. EIS was not influenced by coffee intake, possibly due to its insensibility to evaporating sweat.

In this study, participants' age did not correlate with TEWL. However, MIX values exhibited a trend toward a negative correlation with increasing age at all anatomical locations, but no significant correlation with the MIX value was found. This is in contrast with a previous study, where a significantly higher MIX value was observed in elderly participants (>60 years old) compared to younger ones (20–40 years old), probably due to increased corneocyte size, decreased SC lipid content, and decreased SC moisture content33. It is important to mention that participants' age in our study only ranged from 22 to 65, while a potential decline in skin barrier function may only occur from the age of 60. In general, the effect of aging on skin barrier function remains controversial33-36.

Further, when comparing measurements on the volar forearm and abdomen, no differences in TEWL and MIX values were observed. These findings are in accordance with recent studies showing comparable results of skin barrier function measurements on the volar forearm and abdomen[25,28]. Thus, both the volar forearm and abdomen may be useful anatomical locations to assess skin barrier function in clinical trial settings. From the aspect of practical handling, we found that EIS using the Nevisense device was easier to perform on the volar forearm, due to a lower amount of


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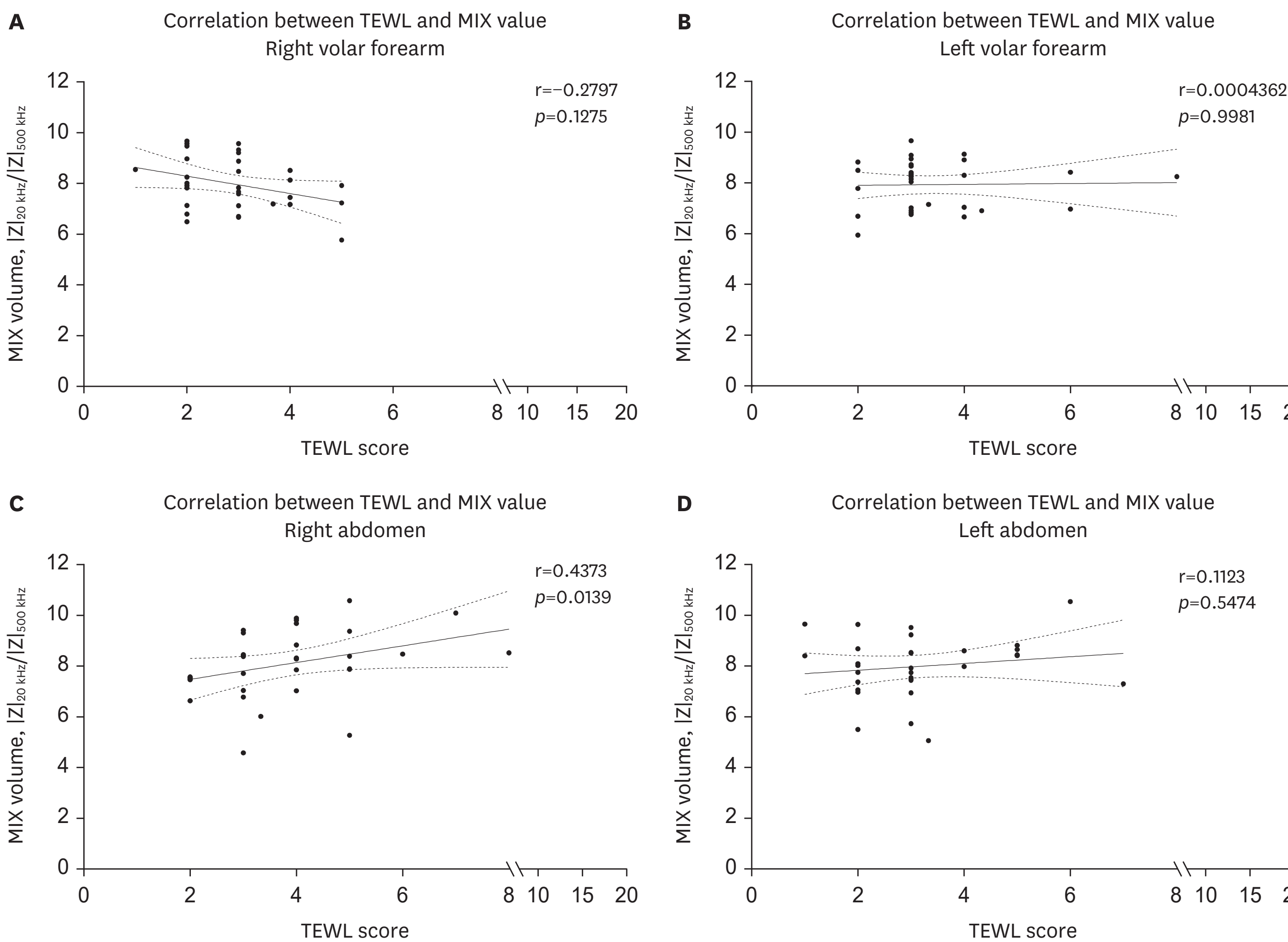


**Fig. 6.** Correlation between TEWL and MIX value. The relationship between TEWL and MIX value was analyzed in healthy individuals (n=31) on the: (A) right volar forearm, (B) left volar forearm, (C) right abdomen, and (D) left abdomen. Each individual point represents the mean value of the reproducible measurements per participant. A simple linear regression with the calculation of the Pearson's correlation coefficient or nonparametric Spearman correlation was used. *p*-values of ≤0.05 are considered significant.
TEWL: transepidermal water loss, MIX: magnitude index.

subcutaneous fat compared to the abdomen. This allowed for more accurate placement of the measuring probe.

No correlation was observed between TEWL and MIX value. Notably, a modest yet statistically significant positive correlation between TEWL and MIX value was observed solely on the right abdomen. In contrast, no significant or pronounced correlation manifested at the other anatomical locations. Given the small sample size, we hereby deduce that the observed correlation on the right abdomen, while statistically significant, may lack substantial clinical significance. These results are in contrast with a recent study conducted by Rinaldi et al.[16], which demonstrates a negative correlation between TEWL and EIS at 1kHz measured after inducing skin barrier damage by the application of cysteine protease papain and trypsin and by tape stripping. The absence of correlation in our study may be attributed to the assessment of TEWL and MIX values on healthy, intact skin, unlike the previous study that focused on damaged skin. In our research, the MIX value was utilized as an indicator to evaluate the skin barrier function. Notably, compared to EIS at 1kHz, the MIX value also encompasses the barrier function of deeper skin layers. This study is the first to assess the correlation between TEWL and MIX value on healthy skin. Given the fact that TEWL measurements and EIS are two distinct biophysical methods for evaluating skin barrier functionality, we are convinced that a combination of these techniques, used side by side, can offer an optimal means of comprehending the functionality of the various elements contributing to skin barrier function. A recent study demonstrated the combined use of TEWL measurements and EIS for evaluating epithelial barrier impairment induced by laundry detergent and sodium dodecyl sulfate[52].

An important limitation of this study was the limited age range (22 to 65) of participants. In future studies, a wider age range should be taken into account. Also, additional factors, including skin type, sex, smoking, and alcohol intake may have an important influence on skin barrier function measurements and should be further investigated. The present study only included healthy individuals, while future studies should also explore the added value of EIS in evaluating skin barrier dysfunction in diseased skin, e.g. ichthyosis, atopic dermatitis, and other forms of eczema. A recent study proved that EIS can detect skin barrier impairment in children with atopic dermatitis[53].

This study confirmed the effect of body cream application, skin washing, moderate to intense physical activity, and coffee intake on TEWL. These factors should therefore be avoided at least 90 minutes prior to TEWL measurements. An acclimatization period of 30 minutes in the standardized room seemed to be sufficient to eliminate the effect of skin washing and physical activity. Body cream application and skin washing also influenced EIS and should therefore be avoided at least 90 minutes prior to these measurements. EIS may be a promising tool for skin barrier function assessment and is less affected by daily routine activities than TEWL.

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**ORCID iDs**

Lisa Huygen
https://orcid.org/0000-0002-8211-0320
Pauline Marie Thys
https://orcid.org/0009-0007-2880-2282
Andreas Wollenberg
https://orcid.org/0000-0003-0177-8722
Jan Gutermuth
https://orcid.org/0000-0002-9252-6004
Inge Kortekaas Krohn
https://orcid.org/0000-0003-3649-1131

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The authors have nothing to disclose.

**DATA SHARING STATEMENT**

The data supporting the findings of this study are available upon request from the corresponding author, Lisa Huygen.

## SUPPLEMENTARY MATERIAL

### Supplementary Table 1

Demographics of the study population

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