Intraday Variations in Skin Water Parameters

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Short Title: Skin water variations

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ABSTRACT

Introduction: Three interrelated skin water assessments include stratum corneum hydration (SCH) via electrical measurements, skin water using tissue dielectric constant (TDC) measurements, and transepidermal water loss (TEWL). These are differentially used for skin physiology research, clinical assessments of dermatological conditions and to assess skin water in diabetes and lymphedema. Often volar forearm skin is used for assessments done at various times of day (TOD). The present goal was to assess the extent of intraday variability in SCH, TDC, and TEWL.

Methods: Twelve medical students self-measured SCH, TDC, and TEWL on their forearm every two hours from 0800 to 2400 hours on two consecutive days. All participants were well-trained and pre-certified in all procedures. Tests for parameter differences among TOD were via the nonparametric Friedman test.

Results: No significant differences in SCH or TEWL were found among TOD over the 16-hour interval for either day or combined. Contrastingly TDC decreased slightly but significantly from morning through evening. There was no evidence of a diurnal pattern. Interestingly, a significant nonlinear relationship between TEWL and SCH was detected.

Conclusion: Findings indicate only minor intra-day variations with TOD trend except for TDC which decreases slightly from morning through evening. The clinical relevance relates to the confidence now gained associated with the parameter estimates when measured at different TOD during normal clinic hours or beyond. This should help in estimating the potential importance of small differences if measured at a different TOD. From a physiological viewpoint, the findings uncover and describe an interesting nonlinear relationship between TEWL and SCH which may serve to propel further investigations that might better characterize this process.

INTRODUCTION

There are three important interrelated skin water assessment measurements. One assesses stratum corneum water hydration (SCH) via stratum corneum electrical conductance or capacitance (SCC) measurements [1, 2] , one assesses skin water from the epidermis through the dermis using tissue dielectric constant (TDC) measurements [3, 4], and one assesses transepidermal water loss (TEWL) [5-7]. Such measurements are differentially used for multiple purposes but broadly for research on aspects of skin physiology [8-11], clinical assessments of dermatological conditions including atopic dermatitis [12-14], psoriasis [15, 16], ichthyosis [17] and wound healing [18-20] and to assess localized skin water in conditions such as diabetes mellitus [21-23] and breast cancer-related lymphedema [24-26]. Often the skin of the volar forearm is used in these assessments [27-31, 2]. Whether done for research or clinical purposes, these skin assessments may be done at various times of day (TOD). Still, there is limited information on the expected intraday variability in the obtained values. Consequentially, it is of basic and clinical interest to help fill this knowledge gap by improving our estimation of the extent of such variability. Some initial ground-breaking efforts have been made to characterize the temporal variability in skin hydration [32-34] as has been recently reviewed [35, 36]. However, there has been limited systematic investigation of the extent of the intraday variation in combined skin assessment parameters. The present report focuses on this issue by assessing SCC, TDC, and TEWL measurements obtained every two hours from 0800 hours to 2400 hours on two consecutive days in 12 healthy young adults.

METHODS

Subjects

Twelve young healthy adult medical students (6 female) participated in this self-measurement research approved by the Nova Southeastern University Institutional Review Board. To be part of the study, subjects needed to agree to be successfully trained in all measurement methods and be willing and able to do these self-measurements at two-hour intervals from 0800 to 2400 hours on two consecutive days of their choice. Exclusions to participation were any skin conditions or open wounds affecting forearm skin which was to be the site of the measurements.

Measurements

All skin water-related measurements were done in triplicate on the non-dominant volar forearm at a location five cm distal to the antecubital fossa as illustrated in **Figure 1**. SCH was assessed by a parameter related to stratum corneum capacitance (SCC) as measured using the MoistureMeterSC (Delfin Technologies, Kuopio, Finland) at a frequency of 1.25 MHz [37]. TEWL ($g/m^2/h$) was measured using the closed chamber VapoMeter (Delfin Technologies, Kuopio, Finland) [38]. TDC was measured with the LymphScanner (Delfin Technologies, Kuopio, Finland) [39]. Skin temperature (TSK) was measured once at the same site using an infrared thermometer (Exergen, Watertown Main, USA, Model DX501-RS)) with a stated repeatability of ± 0.1°C. Measurements were done while the participant was seated with their arm relaxed and comfortably resting palm up on a flat surface, approximately at heart level. The TDC value was obtained at a frequency of 300 MHz with the device functioning as an open-ended coaxial transmission line [40-43]. The TDC value largely depends on water content within the measurement volume [44, 45]. The method has been validated and shown to be reliable [46-48]. Measurements are done by touching skin with one of the probes. TDC and SCH values are displayed in a few seconds after skin contact. TEWL values are displayed after 10 seconds of contact. Further, each participant's whole-body fat and water percentages (FAT% and H20%) were measured using bioimpedance at 50 KHz (InnerScan Body Composition Monitor, Tanita model BC558, The Competitive Edge, Vancouver, WA, USA). Body composition measurements were made with participants barefooted while they stood on a scale for about 10 seconds while gripping handle electrodes. Room temperature (TRM) and relative humidity (RH) were measured (Fluke Model 971, Everett, WA USA with a stated accuracy of ± 0.1°C for TRM and ± 2.5% for RH.

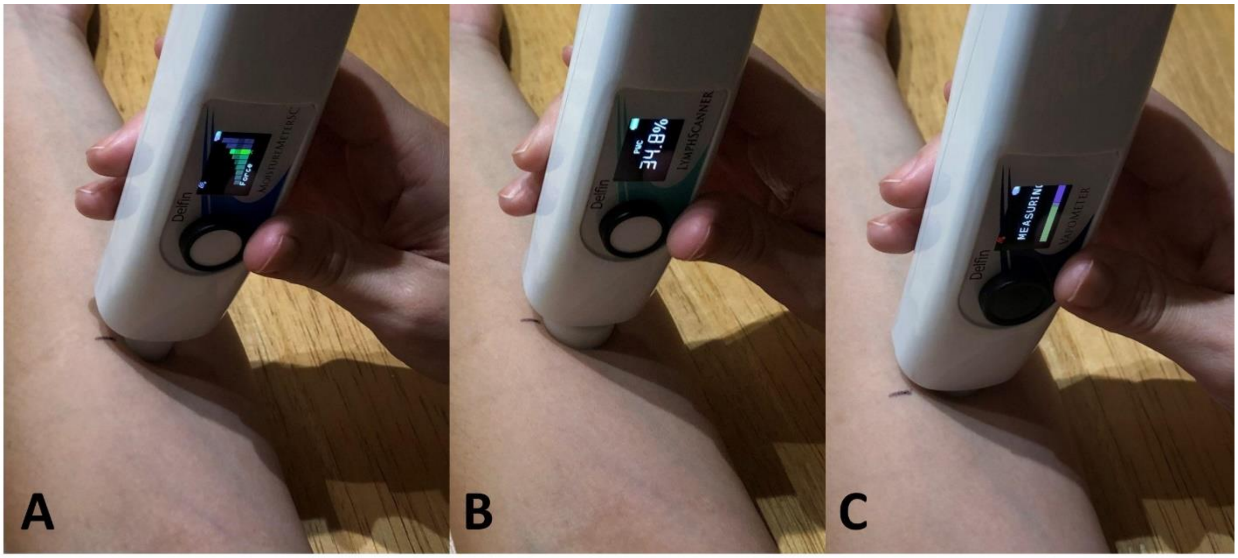

Fig.1. Skin water related measurements

Self-measurements are made in triplicate, five cm distal to the antecubital fossa on the nondominant forearm. Part A shows measurement of stratum corneum hydration (SCH) based on stratum corneum capacitance (SCC) as an index of SCH. The bright bar on the display indicates measurement at the optimum contact pressure. Part B shows measurement of TDC with percentage water shown on the display. Part C shows the measurement of TEWL with the display indicating the measuring process is ongoing at about 70% of the 10 second measurement completed.

Initial Procedures

Before starting self-measurements, each participant was trained and evaluated in the proper use of each skin-measuring device by the author during a dedicated training session. During that session, but following their training, each participant performed a series of measurements that replicated what they would do during their self-measurement protocol. This sequence of measurements was observed for proper technique and corrected if needed, and a second sequence was carried out. No participant required any further corrections. After this training and validation session the total body weight, FAT%, and H2O% were measured.

Self-Measuring Procedure

The self-measurer made their measurements on two consecutive days, usually the weekend, while at home for the entire day. No lotions, creams, or other substances were permitted to be applied to the forearm on measurement days. The sequential order of the self-measurements was TEWL, SCH, TDC, and TSK. TRM and RH were recorded after this measurement sequence. This sequence was repeated every two hours starting at 0800 hours and continuing to and including 2400 hours constituting nine sequential measurement cycles over 16 hours. During the entire sequence, the measurer's activities were confined to normal ones that consisted mostly of studying, watching TV, listening to music, and at times eating and drinking non-caffeinated beverages. Participants were instructed not to eat or drink within one hour of the planned measurement time. However, there were no restrictions placed on what they could eat. No vigorous activity was permitted nor was washing of the forearm permitted. The entire procedure was replicated the next day.

Analysis

The triplicate values of TEWL, SCH, and TDC at each of the nine daily measurement times were averaged to yield one value for each measurement time. Tests for normality via the Shapiro-Wilk test at each measurement time indicated that normality could not be assumed for any time for either of the two days. Thus, statistics were based on nonparametric tests. To test for potential differences in TEWL, SCH, and TDC values among the nine measurement times, the nonparametric Friedman test was used. Values for each parameter at each time were compared between day1 and day2 values using the non-parametric Mann-Whitney test. All statistical tests were done using SPSS, version 16. To evaluate if body habitus parameters (BMI, FAT%, H20%) impacted any of the parameters, the per person time average of each parameter was determined ($TEWL_{AVG}$, SCH_{AVG} and TDC_{AVG} were determined as the average over all nine measured times for both days and the correlation among the parameters determined.

RESULTS

Subject Characteristics

Table 1 summarizes the main demographic features of the group. Male and female participants had similar ages that ranged from 22 to 27 years with a mean ± SD of 24.2 ± 1.4 years for the entire group (N = 12). Males compared to females had a greater height and weight ($p = 0.004$) but there was no statistical difference in BMI ($p = 0.394$). However, males had less FAT% and greater H2O% ($p = 0.002$). It was notable that more of the males tended to be overweight than the females (50% vs. 16.7%) according to the BMI classification. For all participants, their non-dominant hand was the left hand. Race/Ethnicity was based on the self-report of participants with participants equally balanced between White, Asian Indian, and Asian Eastern groups.

	Female	Male	Combined
N	6	6	12
Age (years)	23.5 ± 1.0	25.0 ± 1.5	24.2 ± 1.4
Height (cm)	165.9 ± 6.9	177.0 ± 6.1*	171.5 ± 8.3
Weight (Kg)	60.9 ± 10.4	80.0 ± 7.9*	70.5 ± 13.0
BMI (Kg/m^2)	22.0 ± 3.0	23.3 ± 4.0	22.6 ± 3.5
Fat%	32.0 ± 5.2	16.4 ± 3.6*	24.2 ± 9.2
H2O%	49.6 ±3.4	60.5 ± 3.0*	55.0 ± 6.5
BMI Classification			
%Underweight (BMI < 18.5 Kg/m^2)	0	16.7	8.3
%Normal weight (BMI 18.5 -24.9 Kg/m^2)	83.3	33.3	58.3
%Overweight (BMI 25.0 – 30.0 Kg/m^2)	16.7	50.0	33.3
%Obese (BMI > 30 Kg/m^2)	0	0	0
Race / Ethnicity			
%White/Caucasian	33.3	33.3	33.3
%Asian-Indian	33.3	33.3	33.3
%Asian-East	33.3	33.3	33.3

Temperature and Humidity Variation among Time-of-Day

Figure 2 shows the pattern of variation among time-of-day as measured at two-hour increments averaged between day1 and day2. Tests for significant differences among times using the nonparametric Friedman test failed to detect a significant difference in room temperature (TRM), skin temperature (TSK), or room relative humidity (RH) over the 16-hour measurement interval. However, for TSK there was a slight increasing trend from morning to evening ($r = 0.637$, $p = 0.018$). Room temperature (TRM) and relative humidity (RH) showed no trend during the 16 hours. Averaging values over the nine measurement times yielded an overall average ± SD for TRM_{AVG}, TSK_{AVG}, and RH_{AVG} of 23.8 ± 2.1 °C, 32.3 ± 1.2 °C and 50.0 ± 5.0% respectively.

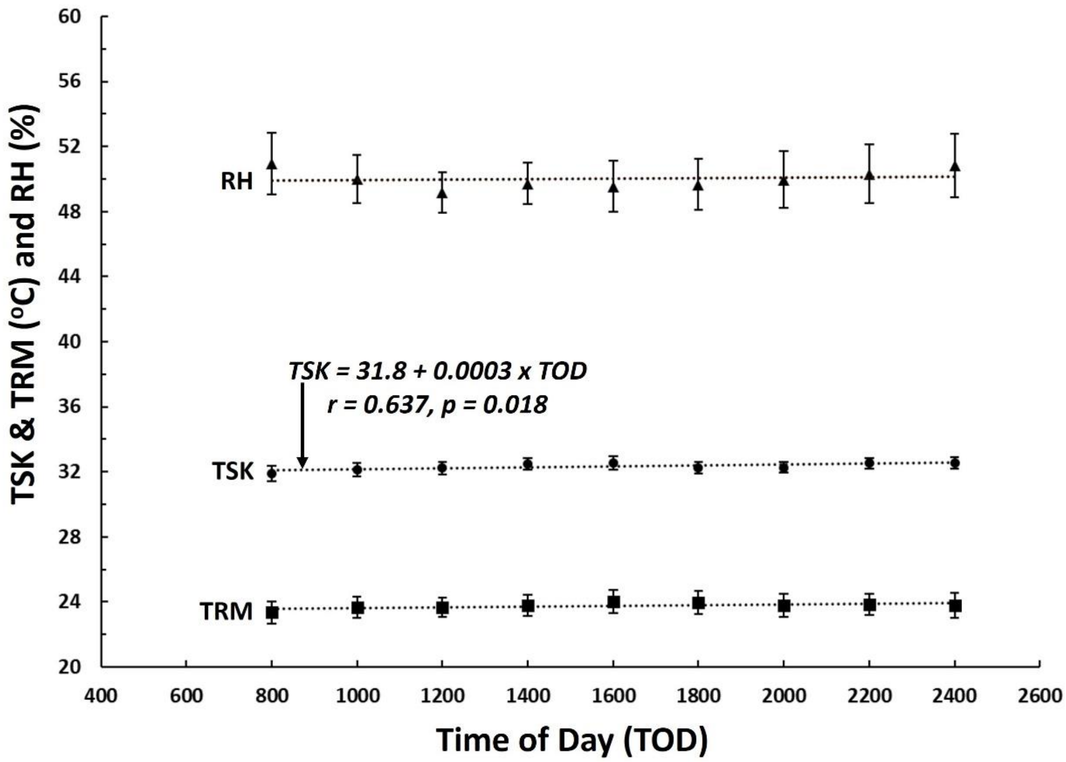

Fig. 2. Environmental parameters

Room temperature (TRM), skin temperature (TSK), and room relative humidity (RH) are shown. Values are two-day averages at each time of day (TOD). Error bars are the standard error of the mean (SEM) and the dotted lines indicate linear regression. The only observed trend was for TSK which demonstrated a slight increase with TOD, as given by the regression equation in the figure. The r is the Pearson correlation coefficient and p is the p-value of the regression.

Day1 vs Day2 TDC Comparisons

Each parameter, TEWL, SCH, TDC, and TSK at each measurement time was compared between day1 and day2 values using the non-parametric Mann-Whitney test. The results showed no significant difference between day1 and day2 values at corresponding times for any of these parameters. The average values for day1 and day2 and the percentage differences between day1 and day2 are summarized in **Table 2**. The percentage difference in TDC at the same times between days was calculated as the day2 **–** day1 difference divided by the average of day1 and day2 values. All average differences in parameters between days were less than 1%. Of the skin water parameters, the smallest standard deviation was noted for the TDC measurement with an SD of ±1.47%. The largest SD was attributable to the SCH measurement which was ± 5.55%.

	Parameter			
	TEWL	SCH	TDC	TSK
Day1	17.3 ± 9.1	14.8 ± 7.6	29.3 ± 4.0	32.3 ± 1.4
Day2	17.2 ± 8.2	14.6 ± 8.7	29.5 ± 3.9	32.3 ±1.3
Percent Difference	0.09 ± 4.71	-0.92 ± 5.55	0.24 ± 1.47	0.04 ± 0.76

Table 2. Inter-day parameter values and percentage differences

Parameter values in this table are determined as the average of all measured times ± SD of 12 subjects (n = 12). The percentage difference is calculated as day1-day2 values divided by the average of day1 and day2 together with ± SD. No parameter values were determined to be statistically different between days.

Parameters by Time-of-Day

Each skin water-related parameter value is shown in **Figure 3** as a function of time of day (TOD). Each value is the average of those obtained on day1 and day2 at corresponding times. There is an overall pattern characteristic of a nearly linear decrease in TDC from morning to night that is expressed by the regression equation TDC = 30.7 – 0.001 x TOD with a Pearson correlation r = -0.885. There was no trend with either TEWL or SC as a function of TOD.

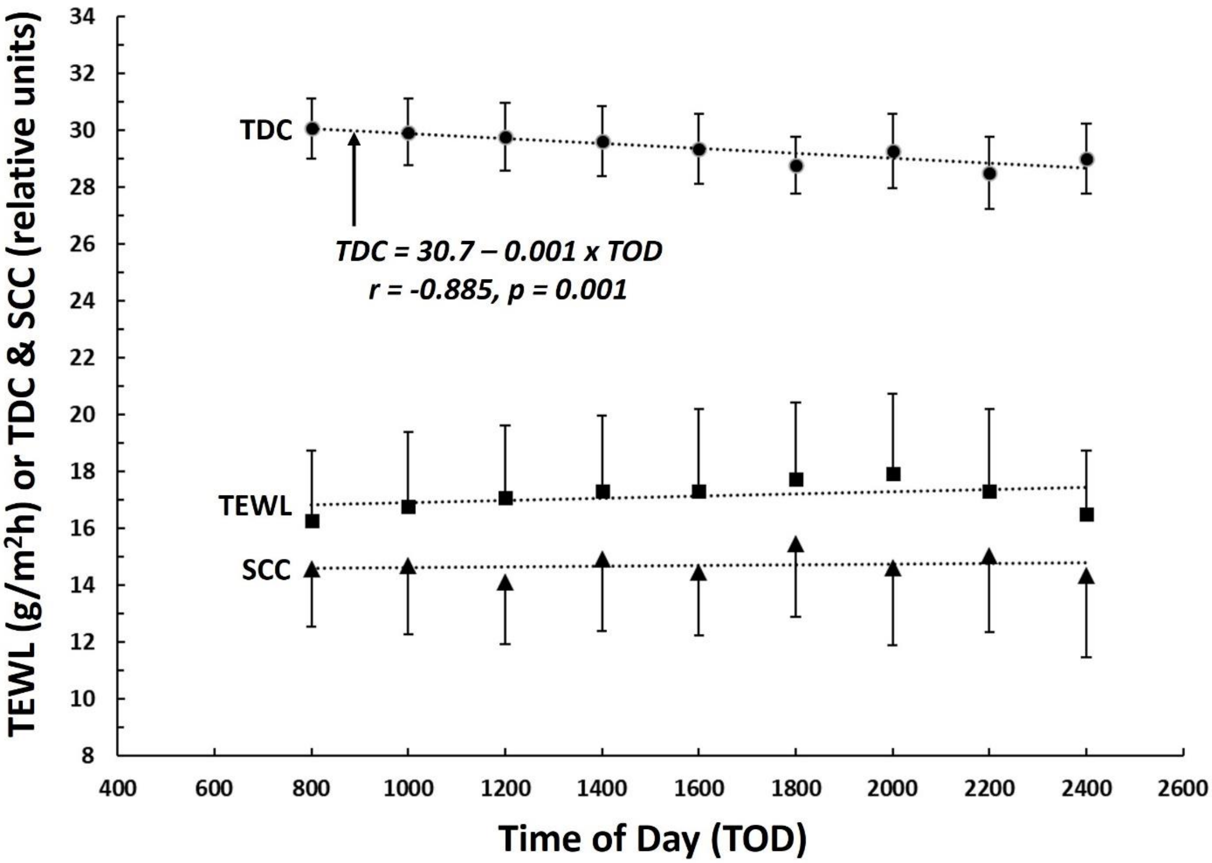

Fig. 3. Skin water related parameters

Tissue dielectric constant (TDC), transepidermal water loss (TEWL) and stratum corneum capacitance index (SCC) are shown. Values are two-day averages at each time of day (TOD). Error bars are the standard error of the mean (SEM) and the dotted lines indicate linear regression. The only observed trend was for TDC which demonstrated a slight decrease with TOD, as given by the regression equation in the figure. The r is the Pearson correlation coefficient and p is the p-value of the regression. The unit for TEWL is g/m^{2}h. TDC is dimensionless, and SCC is expressed in relative units.

TDC Dependence on Body Habitus Parameters

There was no statistically significant correlation between any skin water parameter and a participant's BMI, FAT%, and H2O% values.

Relationship between TEWL and SCH

A significant nonlinear, nearly inverse (1/SCH) relationship between TEWL and SCH was discovered as shown in **Figure 4**. This relationship is characterized by the regression equation TEWL = 170 x $SCH^{-0.967}$. The pattern of this relationship indicates that, except for a few outliers, TEWL remains relatively constant for SCH values greater than about 13. For lower SCH values there is an associated sharp increase in TEWL.

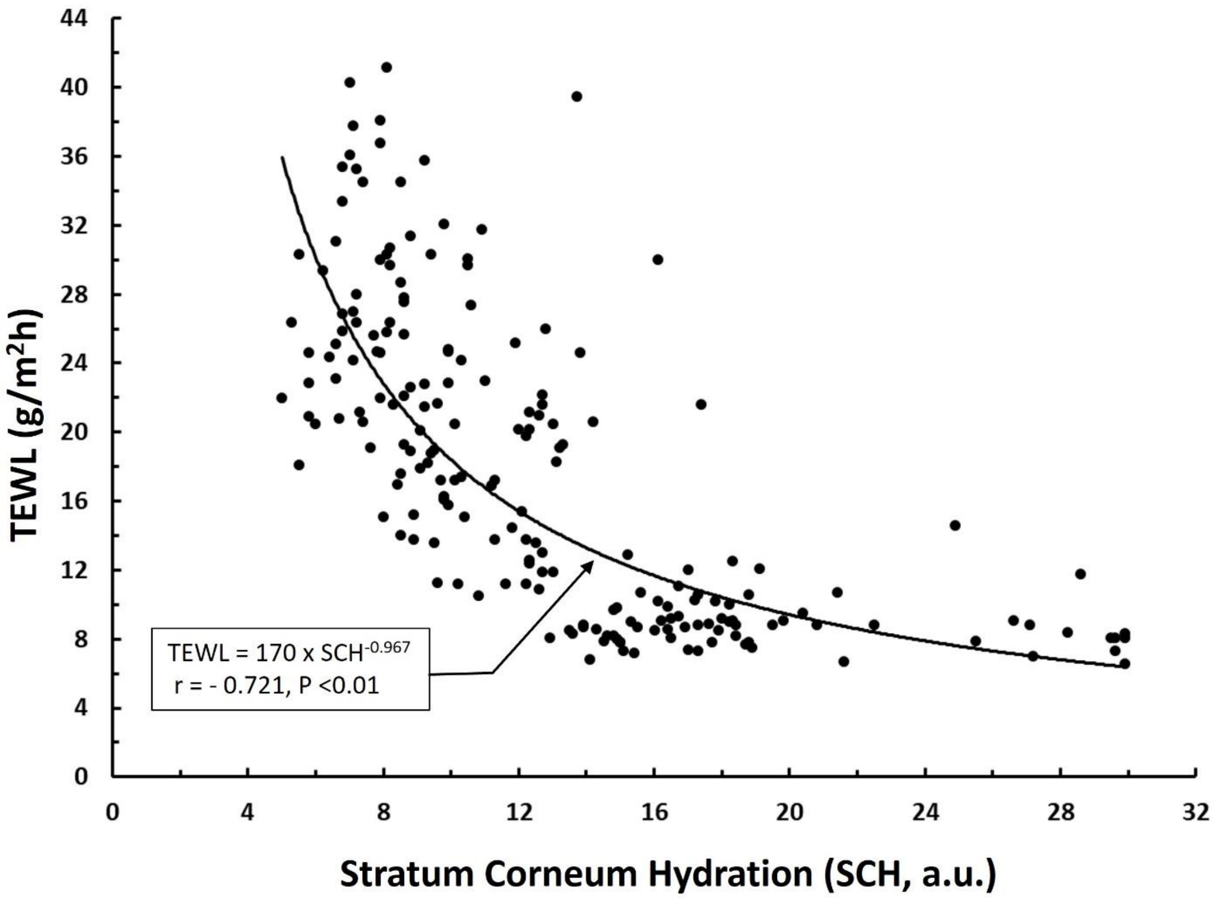

Fig. 4. ***Relationship between transepidermal water loss and stratum corneum hydration***

Data points (N = 216) include all measured TEWL – SCH pairs. Solid line is the nonlinear regression with its equation and parameters shown in the figure.

In contrast to that pattern, there was a direct significant relationship (r = 0.636, p<0.001) between TEWL and TDC as shown in **Figure 5** with the corresponding regression equation expressed as TEWL = 25.5 + 1.54 x TDC. It may be that the nonlinear relationship depends in part on the presence of bound water molecules within the stratum corneum as has been suggested [49].

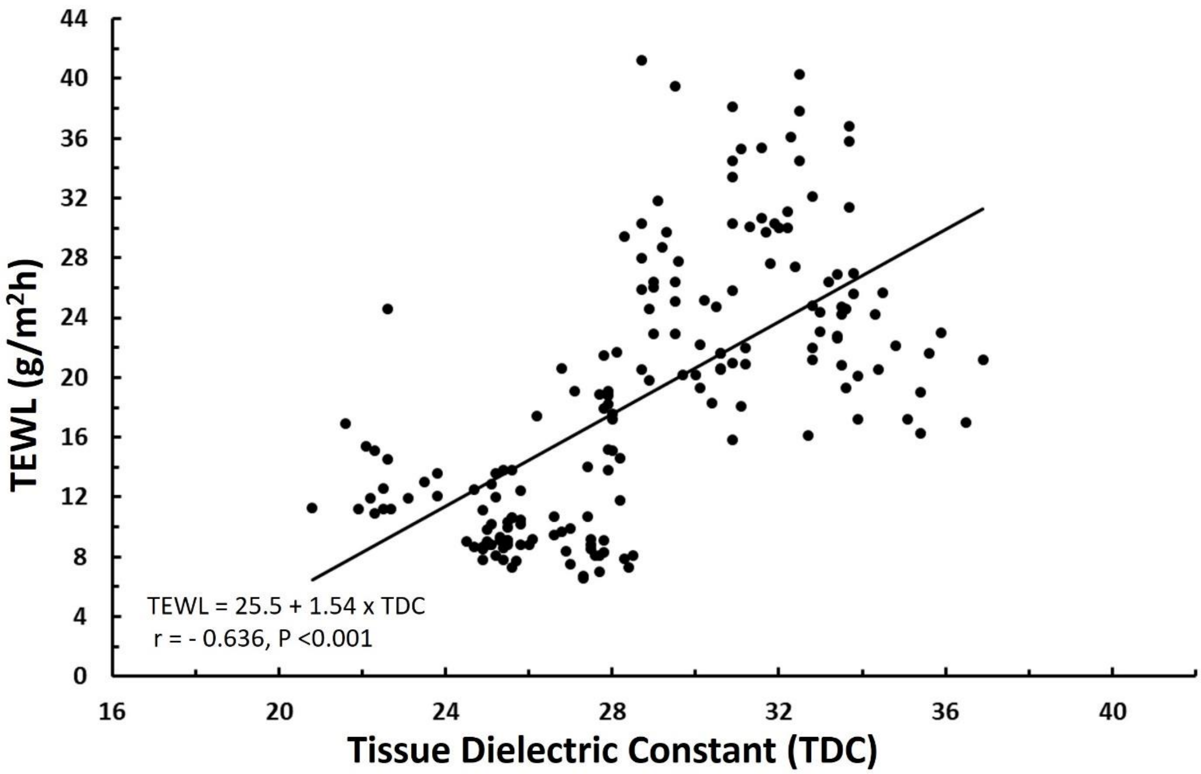

Fig. 5. ***Relationship between transepidermal water loss and tissue dielectric constant***
Data points (N = 216) include all measured TEWL – TDC pairs. Solid line is the linear regression with its equation and parameters shown in the figure.

Gender Comparison

Figure 6 shows the comparison between females and males concerning TEWL values by TOD**.** Male values tend to be larger than females at every TOD but are not statistically different based on Mann-Whiney tests. Friedman tests of male and female TEWL values among TOD shows no significant difference for females (p = 0.418) or for males (p =0.249).

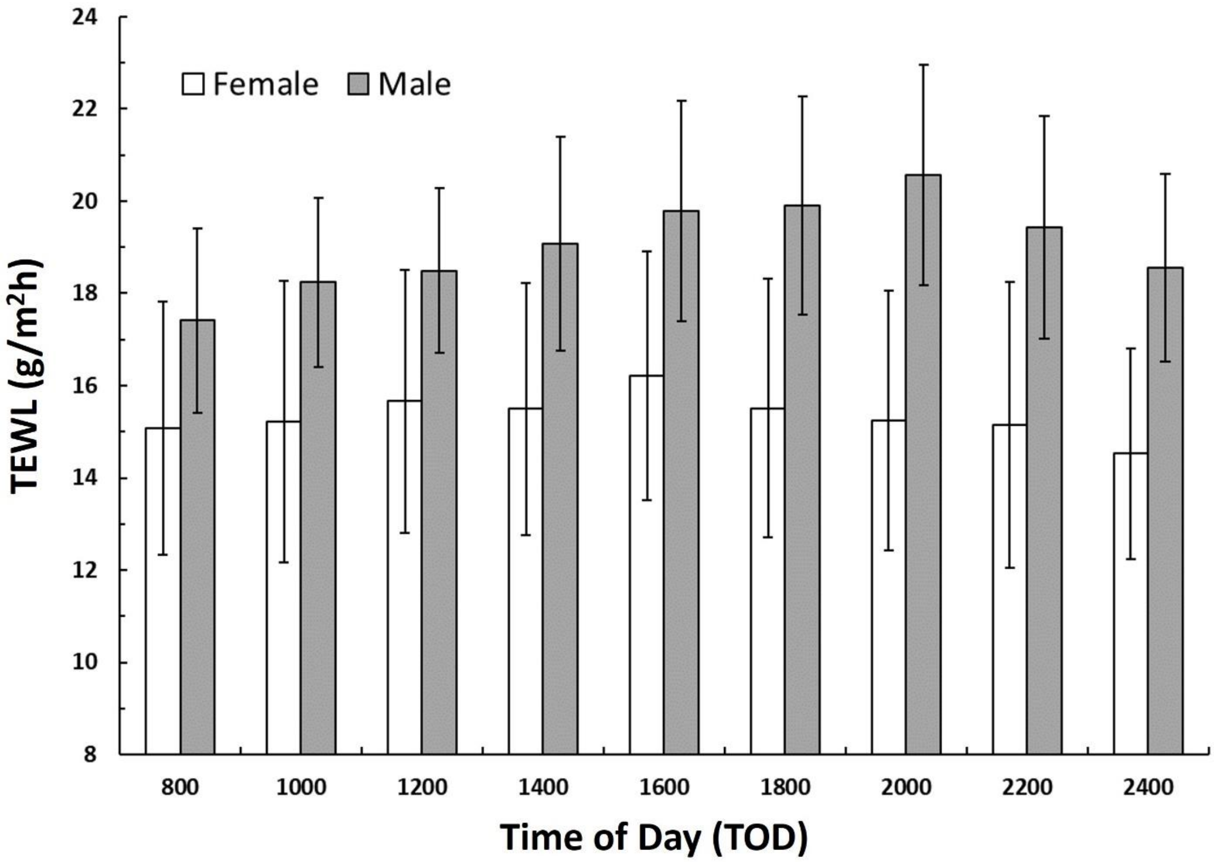

Fig. 6. Gender comparisons for transepidermal water loss

Bars are mean and error bars are standard error of the mean (SEM). Male values tend to be larger than females at every TOD but are not statistically different. Friedman tests of male and female TEWL values among TOD shows no significant difference for females (p = 0.418) or for males (p =0.249).

DISCUSSION

Water within the stratum corneum is distributed at about 30% at the outer layer and about 70% at the deeper parts [30] and among other aspects importantly impacts the mechanical properties of skin [50-52]. It has been pointed out that a large percentage of water within healthy skin is tightly bound to other proteins and thus the use of skin dielectric constant measurements reflects both free and bound water status [53, 54]. This is true of both young and elderly persons but in photoaged skin, there appears to be a shift, with less water being bound and therefore an increase in free water [55]. There is also some evidence of an increase in skin's free water percentage with increasing age in males [56]. SCH has been evaluated in elderly persons in which low levels of forearm SCH were reported to correlate with proinflammatory serum cytokines [57]. Changes in SCH with treatment of atopic dermatitis in adults have been suggested as a marker for treatment outcomes [58] whereas improvements in SCH in children with atopic dermatitis correlated well with improvement in associated pruritus [59] and changes in SCH have been reported as the best indicator of surfactant-related irritation [60]. Thus, the importance of obtaining proper SCH values in clinical assessments is clear as is the proper understanding of the impact of SCH on SC structure and water flux [61]. Similar concepts apply to measurements of TEWL and TDC and possible linkages between SCH and TEWL in healthy skin [2] and the use of both TEWL and SCH in atopic dermatitis [62].

The possibility of a diurnal variation in TEWL was suggested by Shahidullah and co-workers in 1969 based on measurements in six healthy individuals at three time points during the day: 0900, 1400, and 1900 hours [63]. In five of the six subjects TEWL was measured to be greater at both later hours compared to the morning value. The estimated mean increase was 0.048 mg/cm^2/h (0.48 g/m^2/h). In comparison to the present findings, this amount of change is within the standard error of a TEWL measurement as shown in Figure 3 and the prior findings may not properly be interpreted as a diurnal change. TEWL measurements twice daily over many days led to Spruit speculating in 1971 that diurnal changes in TEWL were related to skin temperature changes [64]. in the present study, some skin temperature changes occurred over the 16-hour interval with a slightly increasing trend from 0800, with an average ± SEM TSK of 31.9 ± 0.35 ^{o}C, through 2400 at which TSK was 32.5 ± 0.35 ^{o}C. Furthermore, a comparison of 0800 TEWL (16.0 ± 1.7 g/m^2/h vs. 2400 TEWL (16.5 ± 1.6 g/m^2/h) indicates that the corresponding mean change in TEWL (0. 5 g/m2/h) is within the SEM among subjects. Thus, it is unlikely that intrinsic or temperature-related factors are at work in the present setting indicating a diurnal variation.

In contrast to the present findings that indicate a reasonably stable TEWL throughout the 16-hour, two-day study, data from a 1996 study indicate an 18-21% decrease in TEWL at 1400 hours compared to values measured at 0400 [65]. In this chronobiology study, 16 Caucasian women with ages ranging from 19 to 39 years had forearm TEWL measurements done five times per day from 0400 to 2300 over a two-day interval. Perhaps a difference in findings is attributable to the fact that only females were evaluated whereas the present study included both males and females and also was not restricted to a single racial/ethnic grouping. To test the gender aspect the present data for TEWL was examined for each sex separately as shown in Figure 6 and although male values tended to be greater than female, the TOD stability was similar for both groups. Another study evaluated forearm TEWL values in 12 young adults (three male) of Middle Eastern residence at three time points, 0800, 1200, and 1600 hours [66]. They reported that there was no significant difference in TEWL or SCH among these three times, a result that, for the fewer times evaluated, would be consistent with the present findings [66].

Concerning prior studies concerning intraday variations in TDC, calf measurements made every two hours in 10 young adults from 0800 to 2000 showed a statistically significant linear increase representing about a 5.7% overall increase [67]. It was suggested that this was mainly attributable to fluid redistribution from the upper to lower body. The present results for the forearm indicate a small but statistically significant decrease representing an overall mean reduction of about 2.7% that is also likely due at least in part to fluid redistribution. There has been other evidence consistent with a reduction in skin water from morning to afternoon based on skin ultrasound measurement changes in skin thickness [68]. In that study of 40 young adults (20 male), skin thickness was measured twice, once in the morning between 0830-1030 and again between 1530 - 1700. Skin thickness of the forearm was reported to decrease in both groups and this change was attributed to a diurnal redistribution of water. Skin thickness was also measured on face areas which showed a similar finding but an opposite one when measured on the lower extremities. Another study used ultrasound low echogenicity patterns as an index of skin water and also reported patterns consistent with diurnal changes in 22 young adults but not in 22 elderly persons [32]. In these studies, skin water content was not measured. In a small study of 12 females skin water was self-measured from TDC measurements to a single depth of about 2.0 mm on a single day every hour between 0800 and 2000 [36] . In that study, both facial and forearm skin water decreased from morning to evening whereas lower extremity skin water increased. The present results extend these prior findings concerning intra-day and inter-day forearm skin water changes based on direct TDC measurements as well as co-measured TEWL and SCH.

Additional relevant findings were the demonstration of a significant nonlinear relationship between TEWL and SCH as shown in Figure 5, and a positive relationship between TEWL and TDC as shown in Figure 6. One interpretation of the TEWL-SCH empirical relationship is that a reduction in SCH due to increased TEWL is accelerated at reduced SCH levels, thus perhaps accounting for the nonlinear dependence. Another aspect of that relationship is that the acceleration seems to occur at a SCH value of about 14 a.u. almost in a threshold-like manner. A threshold-like behavior has also been reported for measurements on hand thenar eminence that has much higher TEWL values [2]. The TEWL-TDC relationship, for the present group, indicates that a greater TDC is associated with a greater TEWL. Based on the r^2 value of the relationship (0.405), about 40% of the variation in TEWL with TDC is explained. It is unclear if increased TDC with its associated increased amounts of dermal water is in part driving the observed TEWL increase.

Study limitations

One limitation to be considered is that the data obtained is based on self-measurements done by multiple persons. Although each participant was well trained and certified in the measurement and protocol process by the author, this does not guarantee that, when not observed, errors may occur. However, the consistency of the overall data among all participants, which was carefully reviewed, indicates that any deviations would have been small and limited in overall effect.

Another limitation is the number of participants and their demographics. The present findings apply specifically to the young adult healthy population herein studied and potential generalizations to either older populations or persons with any skin condition must await further investigation. Such temporal studies could use the present results as baseline indicators.

CONCLUSION

Skin tissue water-related parameters (TEWL, SCH, and TDC) assessed every two hours from 0800 to 2400 on two consecutive days indicate only minor intra-day variations with no time-of-day trend except for TDC that decreases slightly from morning through evening. The explanation for this decreasing trend is not provided by the present data but it is suggested that it may represent fluid redistribution from upper to lower body. In part, the clinical relevance of the findings relates to the confidence level associated with the various skin water parameter estimates when measured at different times of day during normal clinic hours or beyond. Thus, the present findings document the amount of variation to be expected which should help in estimating the potential importance of small differences if measured at a different time of the day. Further, there is no evidence for a diurnal variation pattern in the present group of young adults that would suggest one TOD is better than another for such assessments. From a physiological viewpoint, the findings uncover and describe an interesting nonlinear relationship between TEWL and SCH which may serve to propel further investigations that might better characterize this process.

Acknowledgments

The author wishes to thank the participants for their dedication to this research without which this study would not be successful. This research study was unfunded.

Statements of Ethics

This study protocol was reviewed and approved by the Institutional Review Board of Nova Southeastern University with approval number 2021-550 and was classified as an exempt study not requiring written informed consent

Conflict of Interest

The authors have no conflicts of interest to declare.

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This study was not supported by any sponsor or funder.

Author Contributions

The study was designed, overseen, and data analyzed by HNM. HNM also wrote the entire manuscript.

Data Availability

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants, but are available from the corresponding author, (HNM), upon reasonable request.

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