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Nongrafted Skin Area Best Predicts Exercise Core Temperature Responses in Burned Humans

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Abstract

Grafted skin impairs heat dissipation, but it is unknown to what extent this impacts body temperature during exercise in the heat.

PURPOSE—We examined core body temperature responses during exercise in the heat in a group of individuals with a large range of grafts covering their body surface area (BSA; 0-75%).

METHODS—Forty-three individuals (19 females) were stratified into groups based upon BSA grafted: Control (0% grafted, n=9), 17-40% (n=19), and >40% (n=15). Subjects exercised at a fixed rate of metabolic heat production (339 ± 70 W; 4.3 ± 0.8 W/kg) in an environmental chamber set at 40°C, 30% RH for 90 min or until exhaustion (n=8). Whole-body sweat rate and core temperatures were measured.

RESULTS—Whole body sweat rates were similar between groups (Control: 14.7 ± 3.4 ml/min, 17-40%: 12.6 ± 4.0 ml/min, and >40%: 11.7 ± 4.4 ml/min, $P > 0.05$), but the increase in core temperature at the end of exercise in the >40% BSA grafted group ($1.6 \pm 0.5^\circ\text{C}$) was greater than the 17-40% ($1.2 \pm 0.3^\circ\text{C}$) and Control ($0.9 \pm 0.2^\circ\text{C}$) groups ($P < 0.05$). Absolute BSA of non-grafted skin (expressed in m^2) was the strongest independent predictor of the core temperature increase ($r^2 = 0.41$). When re-grouping all subjects, individuals with the lowest BSA of non-grafted skin

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(<1.0 m²) had greater increases in core temperature (1.6±0.5°C) than those with >1.5 m² non-grafted skin (1.0±0.3°C, P<0.05).

CONCLUSIONS—These data imply that individuals with grafted skin have greater increases in core temperature when exercising in the heat and that the magnitude of this increase is best explained by the amount of non-grafted skin available for heat dissipation.

Keywords

Thermoregulation; Split-Thickness Graft; Heat; Thermoregulation

INTRODUCTION

Medical advances have increased the survival rate of individuals with large proportions of their body surface area (BSA) burned. However, burn survivors returning to occupations that require physical exertion in hot environments, such as the military, may be subjected to disproportionate increases in core temperature (6, 15, 20, 25, 28). Severe burns that require split-thickness grafts involve excision of the epidermis and all (or part) of the dermal layer. As a result, the grafted skin has a disrupted vascular bed and associated neural connections along with sweat gland ducts that are removed or disrupted (1, 8, 10, 24). This means that grafted skin fails to increase skin blood flow and produce sweat during heat stress, as previously observed (12). Subsequently, whole body heat loss is impaired (15), potentially resulting in dangerous levels of hyperthermia when such individuals are exercising in the heat (6, 20, 25, 28).

The magnitude of impaired heat loss and the degree of hyperthermia in individuals with grafted skin during exercise is likely dependent on several factors. The amount of BSA grafted has been proposed as an important factor influencing the degree of hyperthermia, but supporting evidence is conflicting (5, 28). For example Austin et al. (5) observed that individuals with as little as 35% and as much as 90% of their BSA grafted had similar changes in core temperature during exercise in a warm environment. Shapiro et al. (28) observed that a larger BSA of burned skin led to greater increases in core temperature during exercise, but the sample size was small (n=10; n=4 in those with >40% BSA burned) and range of % BSA burned was relatively limited (20-55% BSA grafted). An additional factor contributing to the lack of consistency regarding the effect of skin grafts on thermoregulation is likely related to methodological controls (5, 28). Given that increases in core temperature during exercise depend upon the balance between the rate of metabolic heat production and the rate of heat dissipation, it is important to clamp the rate of metabolic heat production between individuals when comparisons are made between groups (14, 19). With metabolic heat production controlled, any differences in core temperature can more precisely be attributed to differences in heat dissipation (i.e., thermoregulation). Doing so, we recently presented a case report of severely impaired whole-body heat dissipation in an individual with 75% of BSA grafted, which ultimately led to greater hyperthermia compared to matched controls (15). Matching heat production to assess heat dissipation is also applicable for field-settings because many occupational tasks require a fixed energy cost (i.e., absolute metabolic heat production) independent of physical characteristics and/or fitness levels (18).

Given conflicting evidence for the degree of thermoregulatory impairment in individuals having low to moderate amounts of BSA grafted and the sheer lack of data for individuals with large amounts of grafted skin (e.g., >55% BSA grafted) (6, 20, 25, 28), the overall purpose of the present investigation was to examine core temperature responses of individuals with well-healed grafted skin (at least 12 months since the last surgery) during exercise in the heat. By using a relatively large number of subjects with a large range of BSA grafted (17-75%, which encompasses approximately 20% of the skin graft population (3)) and having subjects exercise at a fixed rate of metabolic heat production, we tested the hypothesis that individuals with greater amounts of grafted skin would have larger increases in core temperature during exercise in the heat relative to control, non-grafted individuals.

Although the % BSA of grafted skin is the primary clinical variable used to evaluate the severity of the injury, other factors, such as the amount of skin available for heat dissipation (i.e., non-grafted skin), may be more important when assessing an individual's risk for hyperthermia during exercise in the heat. Given this, a secondary aim of this study was to examine if the magnitude of non-grafted BSA better predicts the core temperature increase during exercise in the heat. Specifically, we hypothesize that the absolute amount of non-grafted skin would be a significant predictor of core temperature increases during exercise in the heat.

METHODS

Subjects, free of any known cardiovascular, metabolic, neurological, or psychological diseases, were recruited from North America and tested in Dallas, Texas. Subjects taking medications known to affect the cardiovascular system and/or heat dissipation were excluded. Each subject was fully informed of the experimental procedures and possible risks before giving informed, written consent. The experimental protocol and informed consent were approved by the Institutional Review Boards at the University of Texas Southwestern Medical Center at Dallas and Texas Health Presbyterian Hospital of Dallas.

Thirty-four otherwise healthy burn survivors with grafted skin and nine non-burned control subjects completed this study. Total BSA was calculated from height and weight (13). The burn survivors were stratified into two groups based upon their calculated BSA grafted using the Rule of Nine's (26): 17-40% (n=19) and >40% (n=15). Relative (%) non-grafted skin was calculated by subtracting % BSA grafted from 100. The % BSA grafted cutoffs were selected for convenience to: 1) balance the number of subjects per group; 2) ensure similar physical characteristics between groups, and; 3) be consistent with the U.S. Army cutoffs used for medical exclusionary criteria (4). Absolute surface area (m²) of grafted skin was calculated by multiplying the percentage of grafted skin by total BSA. Non-grafted skin (m²) was calculated by subtracting grafted skin surface area from total BSA. Subject characteristics are in Table 1.

Protocol. Subjects arrived at the laboratory euhydrated (confirmed via urine specific gravity: 1.015 ± 0.008) and having refrained from strenuous exercise, alcohol and caffeine for the 12 h prior. To ensure that all heat loss occurred through the evaporation of sweat, testing was conducted in an environmental chamber at $39.7 \pm 1.0^{\circ}\text{C}$, $31 \pm 3\%$ RH. During

all trials a fan was directed at the subjects to provide an air velocity of ~3 m/s. Subjects were instructed to drink 12 ml/kg of warmed water ($37.1 \pm 1.4^\circ$) throughout exercise (total volume: 951 ± 173 ml). The timing of drinking was carefully controlled such that no fluid was permitted within 5 min of measuring core temperature, preventing the water temperature from influencing the measurement of core temperature. Most subjects performed the first 45 min of exercise on a cycle ergometer ($n = 41$). For the last 45 min of exercise, 17 subjects remained cycling and the others ($n = 26$) walked on a treadmill. Regardless of exercise modality, rate of metabolic heat production was fixed at the same absolute level (~340 W) for all subjects (see Results). Furthermore, the three subject groups had similar physical characteristics. A fixed rate of absolute metabolic heat production, combined with similar physical characteristics (i.e., body mass) between groups ensured that differences between groups in core temperature elevation during exercise could be safely ascribed to differences in the amount of grafted skin, as opposed to potential differences in physical fitness (17), exercise modality, or body morphology (9). Subjects exercised for 90 min and had the option to take a short (5 ± 3 min) break at 45 min. A few subjects elected not to take this break (non-burned controls: 2; 17-40%: 0; >40%: 3). Measures at min 45 and 50 (just before and 5 min of exercise after the break, respectively) confirm that this short break did not adversely affect our main measures and overall findings (see Results). Subjects exercised for the full 90 min unless they reached volitional exhaustion or their core temperature achieved 39.5°C . Unless otherwise noted, starting at 10 min of exercise, measurements were taken every 10 min with an additional measurement at min 45 of exercise.

Measurements

At least 24 hours prior to the trial, maximal oxygen consumption ($\text{VO}_{2\text{max}}$) was measured via indirect calorimetry (Parvo Medics' TrueOne® 2400, Sandy, UT) by having subjects exercise on an electronically braked ergometer (Lode Excalibur Sport; Lode B.V., Groningen, NL) while breathing through a mouthpiece as previously described for our lab (16).

At least 60 min, but usually more than 8 h prior to experimental testing, each subject swallowed a telemetry pill (HQ Inc., Palmetto, FL, USA) for the measurement of intestinal temperature. Three subjects had contraindications for taking the telemetry pill. In these subjects esophageal ($n=1$) or rectal ($n=2$) temperatures were measured and uncorrected for expected slight differences from intestinal temperature. Esophageal temperature was measured at a depth ~40 cm past the naris, while rectal temperature was measured at a depth ~10 cm past the anal sphincter using a general purpose thermocouple (Mon-a-therm, Mallinckrodt Medical, Inc., St. Louis, MO, USA). Skin temperature was measured on a single non-grafted (all subjects) and grafted (grafted individuals) location, which was usually on the upper arm, chest or back depending on the location of the burn injury. Heart rate was measured using a Polar heart rate monitor (Polar Electro, Kempele, Finland) and/or from a five-lead ECG. Whole-body sweat rate was measured via pre- to post- exercise nude body weight measurements, corrected for fluid consumption and urine output. Ratings of perceived exertion (RPE) were measured using a standard Borg scale (from 6-20) (7).

Thermal perception was measured on a modified 9 point scale where, 4 is described as “Neutral (Comfortable)” and 8 as “Unbearably Hot”, in 0.5 increments (30).

Oxygen uptake (VO_2) was measured after 3 min of exercise and at least every 10 min thereafter to verify the target metabolic heat production was attained. If external workload adjustments were made, VO_2 was remeasured after 3 min to ensure the target rate of metabolic heat production was achieved. Rate of metabolic heat production was calculated by subtracting external work rate (in Watts) from metabolic energy expenditure. External work rate was either provided by the cycle ergometer or calculated when using the treadmill according to following standard formula:

$$W = \text{body mass in kg} \times 9.81 \times (\text{speed in mph} \times 0.44704) \times (\text{grade in \%} / 100)$$

Metabolic energy expenditure (M, in Watts) was calculated from VO_2 and respiratory exchange ratio (RER) during exercise using the formula:

$$M = \{ \text{VO}_2 \times [(((\text{RER}-0.7)/0.3) \times e_c) + (((1-\text{RER})/0.3) \times e_f)] \times 1000 / 60$$

where e_c is the caloric equivalent per liter of oxygen for the oxidation of carbohydrates (21.13 kJ), and e_f is the caloric equivalent per liter of oxygen of fat (19.62 kJ) (23).

The Physiological Strain Index (SI), using HR and core temperature (T_c) at rest and the end of exercise was calculated with the following formula adapted from Moran et al. (22):

$$\text{Physiological SI} = \left[5 * \frac{\text{Ending } T_c - \text{Resting } T_c}{39.5 - \text{Resting } T_c} \right] + \left[5 * \frac{\text{Ending HR} - \text{Resting HR}}{\text{Max HR} - \text{Resting HR}} \right]$$

Resting T_c was measured upon arrival at the laboratory, while max HR was obtained during the $\text{VO}_{2\text{max}}$ test performed at familiarization. A Physiological SI of 0 indicates minimal physiological strain, while a Physiological SI of 10 indicates maximal physiological strain.

Similarly, the Perceptual SI was calculated using rating of Thermal Perception and Perceived Exertion (RPE) at the end of exercise using the adapted formula (29):

$$\text{Perceptual SI} = \left[5 * \frac{\text{Ending TS} - 4}{4} \right] + \left[5 * \frac{\text{Ending RPE} - 6}{14} \right]$$

Similar to the Physiological SI, a Perceptual SI of 0 indicates minimal perceptual strain, while a Perceptual SI of 10 indicates maximal perceptual strain.

To identify whether the magnitude of physiological strain was perceived appropriately, and whether there were differences between groups, we subtracted the Physiological SI from Perceptual SI. Accordingly, a difference of ~0 was interpreted that physiological strain was perceived appropriately.

The rate of core temperature change ($^{\circ}\text{C}/\text{min}$) throughout the entire exercise duration was calculated by dividing the increase in core temperature at the end of exercise by exercise duration. Whole-body sweat sensitivity was calculated as the quotient of whole-body sweat rate and the increase in core temperature during exercise. Given that grafted skin does not measurably produce sweat during heat stress (12), whole-body sweat rate and sweat sensitivity are also expressed relative to the absolute BSA of non-grafted skin.

Statistical analysis

Differences between groups in the magnitude of increase in core temperature during exercise were the primary evaluation. The relationship between increases in core temperature and the BSA grafted or non-grafted (expressed in relative and absolute terms) were examined using independent linear regression. The coefficient of determination (i.e., r^2) of each factor was statistically compared to the current criterion measurement's r^2 (i.e., % BSA grafted) (21). Control subjects were not utilized when examining graft-dependent predictors of the elevation in core temperature, given these are not applicable to this population.

A priori statistical significance was set at $P = 0.05$. IBM SPSS Statistics v21 was used for all analyses. Data are reported as mean $\pm$ standard deviation (SD). A two-way (group $\times$ time) mixed model repeated-measures analysis of variance (ANOVA) was used to test the significance of mean differences for measures obtained over time. A one-way ANOVA between groups was used to examine differences between groups for single point measures. Greenhouse–Geisser corrections were made when the assumption of sphericity was violated. Follow-up t-tests and the Bonferroni alpha correction were used when appropriate.

RESULTS

All nine of the controls and all but one (of 19) in the 17-40% group (due to volitional exhaustion) were able to complete the full 90 min of exercise. By contrast, only eight (of 15) subjects in the $>40\%$ group completed the 90 min of exercise (core temperature 39.5°C : $n=3$; volitional exhaustion: $n=4$).

Rate of metabolic heat production during exercise was similar between groups when expressed in absolute (339 ± 56 , 338 ± 75 and 343 ± 76 W for Control, 17-40%, and $>40\%$ groups, respectively; $P > 0.05$) and relative (4.5 ± 0.7 , 4.1 ± 0.9 , and 4.5 ± 0.8 W/kg body mass, respectively; $P > 0.05$) terms. When expressed as W/m^2 of non-grafted skin, the rate of metabolic heat production was greater in the $>40\%$ group (415 ± 152 W/m^2) versus the Control and 17-40% groups (178 ± 24 and 252 ± 61 W/m^2 , respectively; $P < 0.05$), with W/m^2 not being different between Control and 17-40% groups ($P > 0.05$).

The magnitude of increase in core temperature during exercise differed between groups (i.e., significant interaction $P = 0.006$; Figure 1 Panel A), but these differences were not apparent until after min 30 of exercise. Increases in core temperature were not different between Control and 17-40% throughout exercise ($P > 0.05$). However, at all time points after the initial 30 min of exercise, the increase in core temperature from baseline was greater in the $>40\%$ group versus Controls ($P < 0.05$; Figure 1 Panel A). Moreover, the increase in core

temperature was greater in the >40% group versus the 17-40% group at min 50 and 60 and tended to be greater at min 80 ($P = 0.058$) and 90 ($P = 0.097$).

When only examining the overall change in core temperature during exercise (using the value at the cessation of exercise, regardless of exercise time; Figure 1 Panel B), the 17-40% group tended to have a greater increase than Controls ($P = 0.072$), while the >40% group had a greater increase than both the Control ($P < 0.001$) and 17-40% ($P = 0.005$) groups. The rate of core temperature increase during exercise was similar in the Control and 17-40% group (0.009 ± 0.003 and 0.014 ± 0.003 °C/min, respectively; $P = 0.228$), while both were lower than the >40% group (0.022 ± 0.008 °C/min, $P < 0.001$).

The temperature of non-grafted skin did not differ between groups or over time ($P > 0.05$; Table 2). Grafted skin temperature increased throughout exercise and was greater than that of non-grafted skin at each time point, independent of group ($P > 0.05$, Table 2).

From min 10 to min 45 heart rate did not differ between groups (grand mean 127 ± 23 bpm). After 45 min of exercise, heart rate in the >40% group (153 ± 18 bpm) became statistically greater than the 17-40% (134 ± 17 bpm) and Control groups (130 ± 16 bpm; $P < 0.05$) with the exception that at min 90 it was no longer greater compared to the 17-40% group (135 ± 21 , 140 ± 17 , and 156 ± 15 bpm for the Control, 17-40% and >40% groups, respectively; $P > 0.05$).

Rating of Perceived Exertion (RPE) after 45 min of exercise tended to be lower in Control versus >40% (12 ± 2 vs 14 ± 2 , respectively; $P = 0.054$) but not the 17-40% (14 ± 3 ; $P = 0.297$) groups. After 90 min of exercise, RPE in the Controls was not different from the 17-40% (14 ± 2 vs. 13 ± 2 , respectively; $P = 1.00$) or the >40% (16 ± 3 ; $P = 0.090$) groups. However RPE was lower in the 17-40% group when compared to the >40% group ($P = 0.035$).

Thermal perception was not different between groups at min 45 (5.8 ± 0.6 , 6.2 ± 1.0 , and 6.1 ± 0.6 for Control, 17-40% BSA, and >40% BSA, respectively; $P > 0.05$). At the end of exercise Control thermal perception (5.8 ± 0.8) was similar to 17-40% (6.4 ± 1.1 ; $P = 0.434$) and lower than the >40% group (6.9 ± 0.8 ; $P = 0.043$).

Physiological SI in the >40% group was greater than the other groups ($P < 0.05$; Figure 2). The 17-40% group tended ($P = 0.073$) to be greater than the Control group. Perceptual SI followed the same trend; the >40% SI was greater than the other groups ($P < 0.05$; Figure 2), but the 17-40% group did not differ from the Control group ($P = 0.879$). The difference between Physiological and Perceptual SI within each group was not significantly different between groups ($P > 0.05$).

The evaluation of the various approaches to express sweat rate during exercise are shown in Table 3. Whole body sweat rate (ml/min) and sweat sensitivity when expressed as absolute non-grafted BSA (ml/min/°C/m² non-grafted skin) did not differ between groups ($P > 0.05$). Whole-body sweat rate, when expressed as relative (ml/min/%BSA) and absolute (ml/min/m²) BSA non-grafted, was significantly higher in the >40% group compared to the Control and 17-40% groups ($P < 0.05$). Likewise, sweat sensitivity expressed as %BSA

grafted (ml/min/°C/%BSA grafted) was greater in the 17-40% versus >40% group. Finally, absolute whole body sweat sensitivity (ml/min/°C) for Controls was greater than both 17-40% and >40% groups ($P < 0.05$).

Surface area of non-grafted and grafted skin, expressed both as % and m^2 , were each statistically significant independent predictors of the increase in core temperature during exercise (Figure 3). Given % grafted and non-grafted BSA are the same mathematically (i.e., % non-grafted = 100 - % grafted), it is not surprising they had the same predictive value (explaining 24% of the variance). However, absolute BSA non-grafted (in m^2) was the strongest predictor ($P < 0.001$; explaining 41% of the variance). When compared to the current clinical criterion measure of % BSA Grafted, m^2 of non-grafted skin was the only factor that provided a significant improvement in predicting core temperature at the end of exercise ($P = 0.02$). Based upon that observation, we regrouped all subjects (including the non-burned control subjects) as having low ($<1.0 m^2$; $n = 10$), middle (1.0 - $1.5 m^2$; $n = 20$) or high ($>1.5 m^2$; $n = 13$) absolute non-grafted BSA. Low non-grafted BSA (mean: $0.8 \pm 0.2 m^2$) had a greater core temperature increase ($1.6 \pm 0.5 ^\circ C$) compared to individuals with a high BSA of non-grafted skin ($1.8 \pm 0.2 m^2$ and $1.0 \pm 0.3 ^\circ C$; $P = 0.001$). The group with the intermediate amount of non-grafted skin ($1.2 \pm 0.1 m^2$) had an increase in core temperature ($1.3 \pm 0.4 ^\circ C$) that tended to be greater than the low group ($P = 0.089$) and higher than the group with the greatest amount non-grafted BSA ($P = 0.060$).

DISCUSSION

The aims of this study were to test the hypotheses that 1) individuals with greater amounts of grafted skin have larger increases in core temperature during exercise in the heat relative to control, non-grafted individuals and 2) the amount of non-grafted skin is a significant predictor of core temperature increase during exercise in the heat. These hypotheses are supported by our data showing that individuals with >40% BSA grafted have greater increases in core temperature than individuals with lower extent of skin grafting as well as Controls (Figure 1), and that the absolute BSA of non-grafted skin (expressed in m^2) was the strongest predictor of the magnitude of core temperature increase during exercise in heat (Figure 3).

A unique component of the present study is that both the absolute and relative (to body mass) rates of metabolic heat production were equal between groups during exercise. This allowed us to assess the ability of the individuals to dissipate heat during exercise using core temperature responses (9, 14, 19). This methodology has been utilized by others when examining thermoregulatory differences between sexes, individuals of varying ages, fitness levels, and body weights (2, 9, 14, 19). Core temperature increased to the greatest extent in those with >40% BSA grafted (Figure 1), and those with 17-40% BSA grafted tended to have a greater increase in core temperature relative to Controls, but this did not reach statistical significance. When recalculating metabolic heat production relative to absolute BSA of non-grafted skin (in m^2), it is evident that the >40% group was producing almost twice as much metabolic heat relative to the skin surface area available for heat dissipation (i.e., non-grafted skin). Given that grafted skin has little or no ability to contribute to

thermoregulation (10), this is likely the primary explanation for the greater increase in core temperature observed in this group.

Although whole body sweat rate was similar between groups (Table 3, Column 1), when considering sweat rate relative to the functional skin available to secrete sweat (i.e., non-grafted skin), the >40% group had twice the sweat rate compared to the other groups (Table 3, Columns 2 & 3). This elevated sweat rate could be indicative of an adaptive response of the non-grafted skin in this group, but further testing will have to confirm this given that this group also had a greater drive for sweating (because of greater core temperatures). Regardless, this elevated sweat rate was not sufficient to prevent larger increases in core temperature in this group. There are at least two explanations for this: 1) excess sweat dripped off the body, eliminating it as a source of evaporative cooling for effective heat dissipation or 2) the greater sweat output in non-grafted skin may have migrated to grafted skin but failed to provide evaporative cooling, as evidenced by greater temperature of the grafted skin (Table 2). Regarding the latter point, it is important to note that even if evaporation of this “migrated” sweat was occurring over the grafted skin, it may not be an adequate mechanism to cool the skin (and consequently the underlying cutaneous blood) given there are minimal to no increases in skin blood flow in grafted skin during heat stress (12) and therefore only a minimal amount of blood to cool.

Calculating sweat sensitivity (Table 3, Columns 4-6) allows us to compare the amount of sweat produced per °C increase in core temperature. A lower whole-body sweat sensitivity in the grafted groups (Table 3, Column 4) may indicate a reduced central drive for sweating, the intact sweat glands were operating at maximum output and/or there was less skin available to sweat in the grafted groups, each of which would result in a lower whole-body sweat rate per °C increase in core temperature. To account for less intact sweat glands in the grafted subjects (i.e., differences in the amount of non-grafted skin), we recalculated sweat sensitivity relative to m² of non-grafted skin and showed that sweat sensitivity per m² of non-grafted skin was similar between groups (Table 3, Column 6). This observation implies that non-grafted skin does not compensate for the reduction in surface area available for heat dissipation in grafted individuals and, thus, simply responds the same as the non-grafted skin of Control individuals with each °C increase in core temperature.

Although we do not show evidence for an “adaptation” of non-grafted skin to aid in thermoregulation as a compensatory mechanism, it is possible that this lack of adaptation was due to the mostly sedentary, non-heat acclimatized, nature of these subjects. In non-grafted individuals, repeated heat exposure (i.e., heat acclimatization or acclimation) invokes a strong physiological thermoregulatory adaptation, which includes increased sweating. Shapiro et al. (28), observed similar differences in sweating responses between control subjects and a smaller cohort of grafted individuals, however those subjects were heat-acclimated prior to the evaluation whereas the present subjects were not. Therefore it is possible that heat acclimation affects the sweating responses similarly in non-grafted and grafted individuals, but a longitudinal heat acclimatization study with pre- and post-acclimatization measures is warranted to confirm these findings.

We have demonstrated that those individuals with greater %BSA of grafted skin have greater increases in core temperature, but the correlation between %BSA grafted and the increase in core temperature during exercise is weak to moderate (Figure 3). Given that grafted skin does not contribute to thermoregulation (10-12), we propose that a more accurate approach to assess/predict core temperature responses during exercise in the heat is to consider the quantity of skin available for thermoregulation (i.e., non-grafted skin). Indeed, when examining non-grafted and grafted skin as predictive values for core temperature increases during exercise, the amount of non-grafted skin was a stronger predictor; specifically the BSA in m^2 of non-grafted skin was the strongest predictor, even stronger than relative BSA (%) of non-grafted skin (41% versus 24%, respectively). Physiologically, this makes sense because heat exchange from the body to the environment depends upon absolute skin surface area (i.e., m^2), as opposed to the relative (i.e., percent), available for heat loss. For example, we had two individuals with a similar percent of BSA grafted (~49%) and thus the same percent of non-grafted skin (51%). However one of the individuals had a much larger total BSA (2.5 versus 1.9 m^2). This means that the larger individual had a greater BSA that was non-grafted (1.3 versus 0.9 m^2). This greater BSA available for heat dissipation resulted in a lower core temperature increase during exercise (1.0 versus 1.4°C) despite having the same % BSA grafted. Given this physiological rationale, we regrouped our subjects based on their absolute non-grafted surface area being low, middle, or high (<1.0, 1.0-1.5, and >1.5 m^2 , respectively). Not surprisingly, those with the lowest absolute surface area of non-grafted skin had greater increases in core temperature versus those with the highest m^2 of non-grafted skin. Although these findings parallel those when using % BSA grafted (i.e., highest graft had greatest increases in temperature), using absolute non-grafted surface area provides an alternative, more meaningful classification with a stronger physiological rationale. This is also reinforced by the fact that absolute non-grafted surface area explained approximately twice the variance in the core temperature increase than the next best predictor (Figure 3). These findings have important clinical implications when making decisions about the safety of individuals with significant amounts of grafted skin when exercising in the heat. Further, this calculation is rather straightforward as it only requires calculating BSA from height and weight (13), as well as estimating the amount of skin that is grafted (26), all of which are already obtained clinically. Finally, these data question the applicability of having a fixed cut off (i.e. 40% BSA burned) to exclude an individual from military service or preclude an injured soldier from continued service (1). However, we recognize that regardless of classification method, attempting to predict the safety and ability of individuals to exercise in the heat is cautioned.

Although accurately predicting core temperature during an exercise bout may be impossible, understanding an individual's perception of an exercise task may provide insight into whether or not they are at increased risk for heat illness. Self-selected exercise intensity is dictated by afferent feedback from peripheral sites (e.g., skin, muscle) (33). Specifically, an individual may begin an exercise bout in the heat at a slower pace even before any increases in core temperature (31-33). This implies that an individual, when allowed to self-pace, will regulate intensity to avoid task failure and/or reaching a critical core temperature (27). However, this hypothesis implies intact afferent feedback that is accurately interpreted. It is unknown if individuals with significant amounts of grafted skin are able to self-regulate

exercise intensity to avoid heat-related illness and/or injury. Although the study design did not allow for self-regulated exercise intensity, we measured perception of exercise as a surrogate for the interpretation of exercise heat-stress. We found that between group differences in perceptual strain index were similar to those observed for the physiological strain index (Figure 2). Differences in perceptual strain index also paralleled differences in ending core temperature between groups. Likewise, the differences between perceptual and physiological strain, or lack thereof, did not differ between groups. In other words, although the >40% BSA grafted group had greater increases in core temperature they had proportionally greater increases in perceived exertion and thermal strain. This implies that afferent feedback was appropriate in this group and perhaps, if given the option, they would have self-regulated to a lighter exercise intensity to avoid severe hyperthermia. This is important to note because if an individual is able to properly perceive heat stress and self-regulate workload they may be able to still safely exercise in hyperthermic settings. However, future studies specifically examining perception of exercise and self-regulated exercise intensity in individuals with skin grafts are warranted.

CONCLUSIONS

Using a fixed metabolic heat production, a relatively large sample size, and a large range of grafted skin surface areas, we investigated the effect of skin grafts on core temperature during exercise in the heat. It is evident that individuals with greater amounts of grafted skin have larger increases in core temperature. However, it should be recognized that, as with all physiological responses, individual variations exist such that some subjects with a relatively high amount of grafted skin can still thermoregulate relatively well and vice versa. There is not one single variable that is a perfect predictor of an individual's core temperature response, but absolute amount of non-grafted skin surface area (in m²) was the best predictor, explaining 41% of the variance in core temperature observed. Further, individuals with a non-grafted body surface area <1.00 m² had greater increases in core temperature to a similar metabolic demand relative to those with greater non-grafted surface area. Overall, these findings provide further evidence and quantification of the effects of skin grafts on core temperature during exercise in heat.

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Figure 1.

Change in core temperature from rest throughout exercise (Panel A) and at the end of exercise regardless of exercise duration (N = 43; Panel B). Subjects are classified by % of body surface area (BSA) grafted. Because subjects were unable to complete the 90 min of exercise (or equipment malfunction) N= 42, 42, 43, 41, 43, 40, 42, 38, 36, and 35 from 10-90 min, respectively, in the line graph. †, >40% vs Control (P < 0.05); ‡, 17-40% vs >40% (P < 0.05)

Figure 2. Physiological and Perceptual Strain Index Scores at the end of exercise. See text for further explanation. AU, Arbitrary Units. †, Significantly different than 17-40% ($P < 0.05$); ‡, Significantly different than Control ($P < 0.05$).

Figure 3.

The relationship between change in core temperature during 90 min of exercise in the heat (y-axes) and body surface area (BSA) grafted (Panels A & B), non-grafted (Panels C & D), or total BSA (Panel E) when expressed in relative (%) and absolute (m²) BSA terms (x-axes).

TABLE 1Subject characteristics (mean $\pm$ SD).

	Control	Burn survivors with grafted skin	
		17-40% BSA Grafted	>40% BSA Grafted
Number of subjects (male/female)	9 (4/5)	19 (12/7)	15 (8/7)
Years post burn injury [Median]	n/a	20.8 $\pm$ 15.8 [20.8]	11.8 $\pm$ 9.2 [9.2] [†]
Percentage of BSA Grafted (%)	0	30 $\pm$ 7	54 $\pm$ 11 [†]
Absolute BSA Grafted (m ²)	0	0.59 $\pm$ 0.17	1.02 $\pm$ 0.21 [†]
Absolute BSA Non-grafted (m ²)	1.87 $\pm$ 0.16 [†]	1.36 $\pm$ 0.21	0.89 $\pm$ 0.24 * [†]
Weight (kg)	75.0 $\pm$ 12.1	82.9 $\pm$ 14.6	78.0 $\pm$ 15.2
Height (cm)	172 $\pm$ 7	170 $\pm$ 13	172 $\pm$ 8
Age (y)	32 $\pm$ 10	40 $\pm$ 12	33 $\pm$ 11
Peak oxygen uptake (L/min)	2.9 $\pm$ 0.8	2.5 $\pm$ 0.9	2.5 $\pm$ 1.0

BSA, Body surface area;

* Significantly different than Control (P < 0.05);

[†] Significantly different than 17-40% (P < 0.05).

TABLE 2Mean $\pm$ SD skin temperature ($^{\circ}\text{C}$) during exercise

		10 min of exercise	Last 30 sec of exercise
Control	Non-Grafted Skin	36.3 ± 2.2	35.6 ± 2.8
	Grafted Skin	n/a	n/a
17-40%	Non-Grafted Skin	35.2 ± 1.0	35.4 ± 2.0
	Grafted Skin	35.9 ± 0.8	37.6 ± 1.1
>40%	Non-Grafted Skin	35.5 ± 0.7	36.3 ± 1.4
	Grafted Skin	36.1 ± 1.0	37.5 ± 1.6

No differences between groups or time points for non-grafted skin ($P > 0.05$). Grafted skin temperature increased over time and was greater than non-grafted skin at both time points independent of group ($P < 0.05$).

TABLE 3

Mean $\pm$ SD [Median] sweat rate and sensitivity during exercise in the heat from individuals with varying extent of body surface area (BSA) of grafted skin expressed using differing parameters.

	Whole body sweat rate (ml/min)	Sweat Rate (ml/min/%BSA non-grafted)	Sweat Rate (ml/min/m ² non-grafted)	Whole body sweat sensitivity (ml/min/°C)	Sweat Sensitivity (ml/min/°C/%BSA grafted)	Sweat Sensitivity (ml/min/°C/m ² non-grafted)
Control	14.7 $\pm$ 3.4 [15.6]	0.15 $\pm$ 0.03 [0.16]	7.8 $\pm$ 1.5 [8.2]	18.7 $\pm$ 6.6 [20.8]	n/a	9.9 $\pm$ 3.2 [11.0]
17-40%	12.6 $\pm$ 4.0 [12.8]	0.18 $\pm$ 0.07 [0.18]	9.4 $\pm$ 3.2 [9.1]	11.7 $\pm$ 5.1* [11.4]	0.39 $\pm$ 0.17 [0.34]	8.8 $\pm$ 3.7 [7.7]
>40%	11.7 $\pm$ 4.4 [11.5]	0.27 $\pm$ 0.12* [†] [0.27]	14.2 $\pm$ 6.1* [†] [13.7]	7.7 $\pm$ 3.4* [6.5]	0.15 $\pm$ 0.08 [†] [0.13]	9.0 $\pm$ 3.6 [7.9]

* Significantly different from Control (P < 0.05);

[†] Significantly different from 17-40% (P < 0.05).