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

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ABSTRACT

GANIO, M. S., Z. J. SCHLADER, J. PEARSON, R. A. LUCAS, D. GAGNON, E. RIVAS, K. J. KOWALSKE, and C. G. CRANDALL. Nongrafted Skin Area Best Predicts Exercise Core Temperature Responses in Burned H. *Med. Sci. Sports Exerc.*, Vol. 47, No. 10, pp. 2224–2232, 2015. Grafted skin impairs heat dissipation, but it is unknown to what extent this affects 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 on 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 $\mathrm{W \cdot kg^{-1}}$) in an environmental chamber set at 40°C, 30% relative humidity 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 the groups (control: 14.7 ± 3.4 $\mathrm{mL \cdot min^{-1}}$, 17%–40%: 12.6 ± 4.0 $\mathrm{mL \cdot min^{-1}}$; and >40%: 11.7 ± 4.4 $\mathrm{mL \cdot min^{-1}}$; $P > 0.05$), but the increase in core temperature at the end of exercise in the >40% BSA grafted group (1.6°C ± 0.5°C) was greater than the 17%–40% (1.2°C ± 0.3°C) and control (0.9°C ± 0.2°C) groups ($P < 0.05$). Absolute BSA of nongrafted skin (expressed in square meters) was the strongest independent predictor of the core temperature increase ($r^2 = 0.41$). When regrouping all subjects, individuals with the lowest BSA of nongrafted skin (<1.0 $\mathrm{m^2}$) had greater increases in core temperature (1.6°C ± 0.5°C) than those with more than 1.5 $\mathrm{m^2}$ nongrafted skin (1.0°C ± 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 nongrafted skin available for heat dissipation. **Key Words:** THERMOREGULATION, SPLIT-THICKNESS GRAFT, HEAT

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).

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

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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 more than 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 on 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 the 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 shear 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, nongrafted individuals without grafted skin.

Although the percent 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., nongrafted 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 nongrafted BSA better predicts the core temperature increase during exercise in the heat. Specifically, we hypothesize that the absolute amount of nongrafted 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, TX. 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 nonburned control subjects completed this study. Total BSA was calculated from height and weight (13). The burn survivors were stratified into two groups based on their calculated BSA grafted using the rule of nines (26): 17%–40% (*n* = 19) and >40% (*n* = 15). Relative (%) nongrafted 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 US Army cutoffs used for medical exclusionary criteria (4). Absolute surface area (m^2) of grafted skin was calculated by multiplying the percentage of grafted skin by total BSA. Nongrafted skin (m^2) was calculated by subtracting grafted skin surface area from total BSA. Subjects' characteristics are in Table 1.

Protocol

The 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°C ± 1.0°C, 31% ± 3% RH. During all trials, a fan was directed at the subjects to provide an air velocity of approximately 3 $m \cdot s^{-1}$. Subjects were instructed to drink 12 $mL \cdot kg^{-1}$ of warmed water (37.1°C ± 1.4°C) throughout exercise (total volume, 951 ± 173 mL). The timing of drinking was carefully controlled such that no

TABLE 1. Subjects' characteristics (mean ± SD).

		Burn Survivors with Grafted Skin	
	Control	**17%–40% BSA Grafted**	**>40% BSA Grafted**
Number of subjects (male/female)	9 (4/5)	19 (12/7)	15 (8/7)
Years after burn injury, mean ± SD [median]	n/a	20.8 ± 15.8 [20.8]	11.8 ± 9.2 [9.2]**
Percentage of BSA grafted	0	30 ± 7	54 ± 11**
Absolute BSA grafted, m^2	0	0.59 ± 0.17	1.02 ± 0.21**
Absolute BSA nongrafted, m^2	1.87 ± 0.16**	1.36 ± 0.21	0.89 ± 0.24*,**
Weight, kg	75.0 ± 12.1	82.9 ± 14.6	78.0 ± 15.2
Height, cm	172 ± 7	170 ± 13	172 ± 8
Age, yr	32 ± 10	40 ± 12	33 ± 11
Peak oxygen uptake, $L \cdot min^{-1}$	2.9 ± 0.8	2.5 ± 0.9	2.5 ± 1.0

*Significantly different from the control group ($P < 0.05$).
**Significantly different from the 17%–40% group ($P < 0.05$).

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 (approximately 340 W) for all subjects (see the "Results" section). 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 the 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 (nonburned controls: 2; 17%–40%: 0; >40%: 3). Measures at minutes 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 the "Results" section). 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 minute 45 of exercise.

Measurements. At least 24 h before the trial, maximal oxygen consumption ($\dot{V}O_{2\max}$) 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 laboratory (16).

At least 60 min, but usually more than 8 h before 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 approximately 40 cm past the naris, whereas rectal temperature was measured at a depth of approximately 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 nongrafted (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-exercise to postexercise 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 to 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 ($\dot{V}O_2$) was measured after 3 min of exercise and at least every 10 min thereafter to verify that the target metabolic heat production was attained. If external workload adjustments were made, $\dot{V}O_2$ 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:

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

Metabolic energy expenditure (M, in watts) was calculated from $\dot{V}O_2$ and respiratory exchange ratio (RER) during exercise using the formula:

$$M = \left\{\dot{V}O_2 \times [(((\text{RER} - 0.7)/0.3)\, e_c) + (((1 - \text{RER})/0.3)\, e_f)]\right\} \\ \times 1000/60,$$

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):

$$\text{physiological SI} = \left[5 \times \frac{\text{ending } T_c - \text{resting } T_c}{39.5 - \text{resting } T_c}\right] \\ + \left[5 \times \frac{\text{ending HR} - \text{resting HR}}{\text{max HR} - \text{resting HR}}\right]$$

Resting T_c was measured upon arrival at the laboratory, whereas max HR was obtained during the $\dot{V}O_{2\max}$ test performed at familiarization. A physiological SI of zero indicates minimal physiological strain, whereas a physiological SI of 10 indicates maximal physiological strain.

Similarly, the perceptual SI was calculated using rating of thermal perception (TS) and perceived exertion (RPE) at the end of exercise using the adapted formula (29):

$$\text{perceptual SI} = \left[5 \times \frac{\text{ending TS} - 4}{4}\right] + \left[5 \times \frac{\text{ending RPE} - 6}{14}\right]$$

Similar to the physiological SI, a perceptual SI of zero indicates minimal perceptual strain, whereas 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 approximately 0 was interpreted that physiological strain was perceived appropriately.

The rate of core temperature change ($^{\circ}\mathrm{C}\cdot\mathrm{min}^{-1}$) 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 nongrafted 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 nongrafted (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 clinical criterion measurement's r^2 (i.e., %BSA grafted) (21). Control subjects were not used 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 $P \leq 0.05$. IBM SPSS Statistics v21 was used for all analyses. Data are reported as mean ± standard deviation (SD). A two-way (group × 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 the groups when expressed in absolute (339 ± 56, 338 ± 75, and 343 ± 76 W for the control, 17%–40%, and >40% groups, respectively; $P > 0.05$) and relative terms (4.5 ± 0.7, 4.1 ± 0.9, and 4.5 ± 0.8 $\mathrm{W}\cdot\mathrm{kg}^{-1}$ body mass, respectively; $P > 0.05$). When expressed as $\mathrm{W}\cdot\mathrm{m}^{-2}$ of nongrafted skin, the rate of metabolic heat production was greater in the >40% group (415 ± 152 $\mathrm{W}\cdot\mathrm{m}^{-2}$) versus the control and 17%–40% groups (178 ± 24 and 252 ± 61 $\mathrm{W}\cdot\mathrm{m}^{-2}$, respectively; $P < 0.05$), with $\mathrm{W}\cdot\mathrm{m}^{-2}$ not being different between the control and 17%–40% groups ($P > 0.05$).

The magnitude of increase in core temperature during exercise differed between the groups (i.e., significant interaction, $P = 0.006$; Fig. 1A), but these differences were not apparent until after minute 30 of exercise. Increases in core temperature were not different between the control and 17%–40% groups 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 the controls ($P < 0.05$; Fig. 1A). Moreover, the increase in core temperature was greater in the >40% group versus the 17%–40% group at minutes 50 and 60 and tended to be greater at minutes 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; Fig. 1B), the 17%–40% group tended to have a greater increase than the control group ($P = 0.072$), whereas the >40% group had a greater

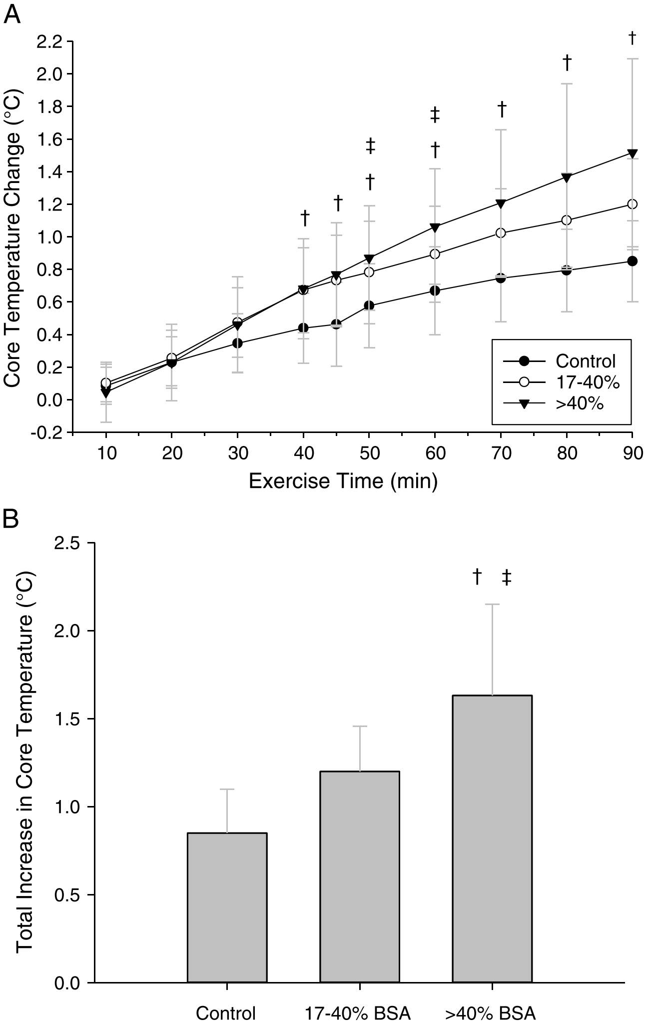

FIGURE 1—Change in core temperature from rest throughout exercise (A) and at the end of exercise regardless of exercise duration (N = 43) (B). Subjects are classified by percent of BSA grafted. Because subjects were unable to complete the 90 min of exercise (or equipment malfunction), n = 42, 42, 43, 41, 43, 40, 42, 38, 36, and 35 from 10 to 90 min, respectively, in the line graph. † >40% vs control ($P < 0.05$); ‡17%–40% vs >40% ($P < 0.05$).

increase than both the control ($P < 0.001$) and 17%–40% groups ($P = 0.005$). 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^{-1}, respectively; $P = 0.228$), whereas both were lower than the >40% group (0.022 ± 0.008°C·min^{-1}; $P < 0.001$).

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

From minute 10 to minute 45, heart rate did not differ between the 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 minute 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 the control versus the >40% group (12 ± 2 vs 14 ± 2, respectively; $P = 0.054$) but not the 17%–40% group (14 ±3; $P = 0.297$). After 90 min of exercise, RPE in the controls was not different from the 17%–40% group (14 ± 2 vs 13 ± 2, respectively; $P = 1.00$) or the >40% (16 ± 3; $P = 0.090$) group. However, RPE was lower in the 17%–40% group when compared to the >40% group ($P = 0.035$).

Thermal perception was not different between the groups at minute 45 (5.8 ± 0.6, 6.2 ± 1.0, and 6.1 ± 0.6 for the 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 that of the 17%–40% group (6.4 ± 1.1; $P = 0.434$) and lower than that of the >40% group (6.9 ± 0.8; $P = 0.043$).

Physiological SI in the >40% group was greater than those of the other groups ($P < 0.05$; Fig. 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 those of the other groups ($P < 0.05$; Fig. 2), but that of the 17%–40% group did not differ from that of the control group ($P = 0.879$). The difference between physiological and perceptual SI within each group was not significantly different between the groups ($P > 0.05$).

TABLE 2. Mean ± SD skin temperature (°C) during exercise.

	10 min of Exercise	Last 30 s of Exercise
Control		
Nongrafted skin	36.3 ± 2.2	35.6 ± 2.8
Grafted skin	n/a	n/a
17%–40%		
Nongrafted skin	35.2 ± 1.0	35.4 ± 2.0
Grafted skin	35.9 ± 0.8	37.6 ± 1.1
>40%		
Nongrafted skin	35.5 ± 0.7	36.3 ± 1.4
Grafted skin	36.1 ± 1.0	37.5 ± 1.6

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

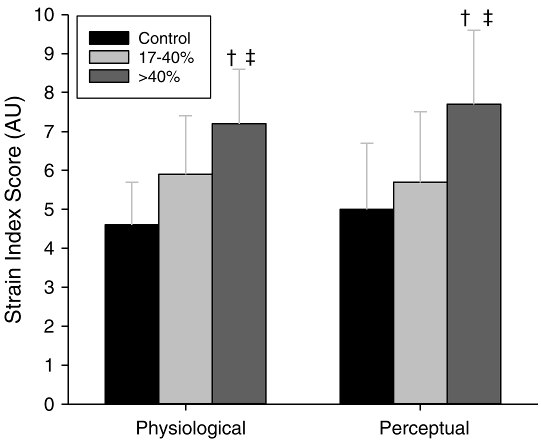

FIGURE 2—Physiological and perceptual strain index scores at the end of exercise. See text for further explanation. AU, Arbitrary units. †Significantly different from the 17%–40% group ($P < 0.05$); ‡Significantly different from the control group ($P < 0.05$).

The evaluation of the various approaches to express sweat rate during exercise is shown in Table 3. Whole-body sweat rate (mL·min^{-1}) and sweat sensitivity when expressed as absolute nongrafted BSA (mL·min^{-1}·°C^{-1}·m^{-2} nongrafted skin) did not differ between the groups ($P > 0.05$). Whole-body sweat rate, when expressed as relative (mL·min^{-1}·%BSA^{-1}) and absolute (mL·min^{-1}·m^{-2}) BSA nongrafted, 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^{-1}·°C^{-1}·%BSA^{-1}) was greater in the 17%–40% versus the >40% group. Finally, absolute whole-body sweat sensitivity (mL·min^{-1}·°C^{-1}) for the controls was greater than for both the 17%–40% and >40% groups ($P < 0.05$).

Surface area of nongrafted and grafted skin, expressed both as percent and square meter, were each statistically significant independent predictors of the increase in core temperature during exercise (Fig. 3). Given percent grafted and nongrafted BSA are the same mathematically (i.e., % nongrafted = 100 − % grafted), it is not surprising that they had the same predictive value (explaining 24% of the variance). However, absolute BSA nongrafted (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, surface area (m^2) of nongrafted skin was the only factor that provided a significant improvement in predicting core temperature at the end of exercise ($P = 0.02$). Based on that observation, we regrouped all subjects (including the nonburned 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 nongrafted BSA. Low nongrafted BSA (mean, 0.8 ± 0.2 m^2) had a greater core temperature increase (1.6°C ± 0.5°C) compared to individuals with a high BSA of nongrafted skin (1.8 ± 0.2 m^2 and 1.0°C ± 0.3°C; $P = 0.001$). The group with the intermediate amount of nongrafted skin (1.2 ± 0.1 m^2) had an increase in core temperature (1.3°C ± 0.4°C) that tended

TABLE 3. Mean ± SD [median] sweat rate and sensitivity during exercise in the heat from individuals with varying extent of BSA of grafted skin expressed using different parameters.

	Whole-Body Sweat Rate (mL·min^{-1})	**Sweat Rate (mL·min^{-1}·%BSA^{-1} Nongrafted)**	**Sweat Rate (mL·min^{-1}·m^{-2} Nongrafted)**	**Whole-Body Sweat Sensitivity (mL·min^{-1}·°C^{-1})**	**Sweat Sensitivity (mL·min^{-1}·°C^{-1}·%BSA^{-1} grafted)**	**Sweat Sensitivity (mL·min^{-1}·°C^{-1}·m^{-2} Nongrafted)**
Control	14.7 ± 3.4 [15.6]	0.15 ± 0.03 [0.16]	7.8 ± 1.5 [8.2]	18.7 ± 6.6 [20.8]	n/a	9.9 ± 3.2 [11.0]
17%–40%	12.6 ± 4.0 [12.8]	0.18 ± 0.07 [0.18]	9.4 ± 3.2 [9.1]	11.7 ± 5.1 [11.4]*	0.39 ± 0.17 [0.34]	8.8 ± 3.7 [7.7]
>40%	11.7 ± 4.4 [11.5]	0.27 ± 0.12 [0.27]*,**	14.2 ± 6.1 [13.7]*,**	7.7 ± 3.4 [6.5]*	0.15 ± 0.08 [0.13]**	9.0 ± 3.6 [7.9]

*Significantly different from control ($P < 0.05$).
**Significantly different from 17-40% ($P < 0.05$).

to be greater than the low group (P = 0.089) and higher than the group with the greatest amount of nongrafted 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 individuals with nongrafted skin, and (2) the amount of nongrafted 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 more than 40% BSA grafted have greater increases in core temperature than individuals with lower extent of skin grafting as well as controls (Fig. 1), and that the absolute BSA of nongrafted skin (expressed in m^2) was the strongest predictor of the magnitude of core temperature increase during exercise in heat (Fig. 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 the 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 used 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 more than 40% BSA grafted (Fig. 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 nongrafted skin (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., nongrafted 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 the groups (Table 3, column 1), when considering sweat rate relative to the functional skin available to secrete sweat (i.e., nongrafted skin), the >40% group had twice the sweat rate compared to the other groups (Table 3, columns 2 and 3). This elevated sweat rate could be indicative of an adaptive response of the nongrafted 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 nongrafted 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 degree Celsius increase in core temperature. 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 degree Celsius increase in core temperature. To account for less intact sweat glands in the grafted subjects (i.e., differences in the amount of nongrafted skin), we recalculated sweat sensitivity relative to the surface area of nongrafted skin and showed that sweat sensitivity per square meter of nongrafted skin was similar between the groups (Table 3, column 6). This observation implies that nongrafted 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 nongrafted skin of control individuals with each degree Celsius increase in core temperature.

Although we do not show evidence for an "adaptation" of nongrafted 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 individuals with nongrafted skin, 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 individuals

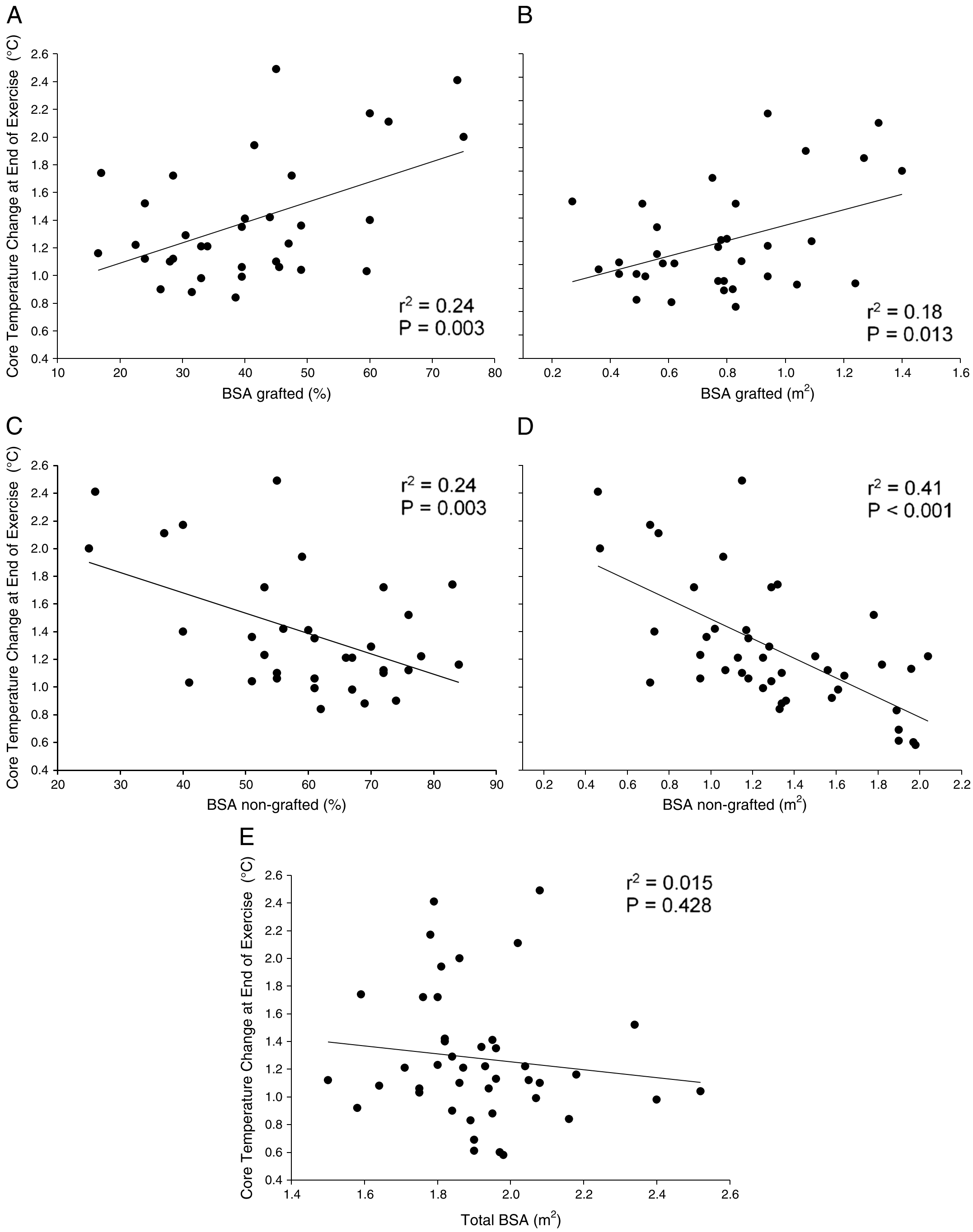

FIGURE 3—Relationship between change in core temperature during 90 min of exercise in the heat (*y*-axis) and BSA grafted (A, B), nongrafted (C, D), or total BSA (E) when expressed in relative (%) and absolute (m^2) BSA terms (*x*-axis).

with grafted skin; however, those subjects were heat-acclimated before the evaluation, whereas the present subjects were not. Therefore, it is possible that heat acclimation affects the sweating responses similarly in individuals with nongrafted skin and those with grafted skin, but a longitudinal heat acclimatization study with preacclimatization and postacclimatization measures is warranted to confirm these findings.

We have demonstrated that those individuals with greater percent BSA of grafted skin have greater increases in core temperature, but the correlation between percent BSA grafted and the increase in core temperature during exercise is weak to moderate (Fig. 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., nongrafted skin). Indeed, when examining nongrafted and grafted skin as predictive values for core temperature increases during exercise, the amount of nongrafted skin was a stronger predictor; specifically, the BSA in square meter of nongrafted skin was the strongest predictor, even stronger than relative BSA (%) of nongrafted skin (41% vs 24%, respectively). Physiologically, this makes sense because heat exchange from the body to the environment depends on 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 nongrafted skin (51%). However, one of the individuals had a much larger total BSA (2.5 vs 1.9 m^2). This means that the larger individual had a greater BSA that was nongrafted (1.3 vs 0.9 m^2). This greater BSA available for heat dissipation resulted in a lower core temperature increase during exercise (1.0°C vs 1.4°C) despite having the same %BSA grafted. Given this physiological rationale, we regrouped our subjects based on their absolute nongrafted 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 nongrafted skin had greater increases in core temperature versus those with the highest surface area of nongrafted skin. Although these findings parallel those when using %BSA grafted (i.e., highest graft had greatest increases in temperature), using absolute nongrafted surface area provides an alternative, more meaningful classification with a stronger physiological rationale. This is also reinforced by the fact that absolute nongrafted surface area explained approximately twice the variance in the core temperature increase than the next best predictor (Fig. 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. Furthermore, 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 cutoff (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 and 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 assumes 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 (Fig. 2). Differences in perceptual strain index also paralleled differences in ending core temperature between the groups. Likewise, the differences between perceptual and physiological strain, or lack thereof, did not differ between the groups. 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 rate of 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 nongrafted skin surface area (m^2) was the best predictor, explaining 41% of the variance in core temperature observed. Furthermore, individuals with a nongrafted body surface area less than 1.00 m^2 had greater increases in core temperature to a similar metabolic demand relative to those with greater nongrafted 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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