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Children with Burn Injury Have Impaired Cardiac Output during Submaximal Exercise

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Abstract

Introduction—Burn trauma damages resting cardiac function; however, it is currently unknown if the cardiovascular response to exercise is likewise impaired. We tested the hypothesis that, in children, burn injury lowers cardiac output (Q) and stroke volume (SV) during submaximal exercise.

Methods—Five children with 49±4% total body surface area (BSA) burned (2 female, 11.7±1 y, 40.4±18 kg, 141.1±9 cm) and eight similar non-burned controls (5 female, 12.5±2 y, 58.0±17 kg, 147.3±12 cm) with comparable exercise capacity (peak oxygen consumption [peak VO_2]: 31.9±11 vs. 36.8±8 ml $O_2 \cdot kg \cdot min^{-1}$, P=0.39) participated. The exercise protocol entailed a pre-exercise (pre-EX) rest period followed by 3-minute exercise stages at 20 W and 50 W. VO_2, heart rate (HR), Q (via non-rebreathing), SV (Q/HR), and arteriovenous O_2 difference ([a-v] $O_{2\ dif}$, Q/VO_2) were the primary outcome variables.

Results—Using a 2-way factorial ANOVA (group [G] × exercise [EX]), we found that Q was ~27% lower in the burned than the non-burned group at 20 W of exercise (burned 5.7±1.0 vs. nonburned: 7.9±1.8 $L \cdot min^{-1}$) and 50 W of exercise (burned 6.9±1.6 vs. nonburned 9.2 ±3.2 $L \cdot min^{-1}$) (G × EX interaction, P=0.012). SV did not change from rest to exercise in burned children but increased by ~24% in the non-burned group (main effect for EX, P=0.046). Neither [a-v] $O_{2\ dif}$ nor VO_2 differed between groups at rest or exercise, but HR response to exercise was reduced in the burn group (G × EX interaction, P=0.004). When normalized to BSA, SV (index) was similar between groups; however, Q (index) remained attenuated in the burned group (G × EX interaction, P<0.008).

Conclusions—Burned children have an attenuated cardiovascular response to submaximal exercise. Further investigation of hemodynamic function during exercise will provide insights important for cardiovascular rehabilitation in burned children.

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Introduction

Burn trauma causes a profound activation of the sympathetic autonomic nervous system that prompts the classic fight-or-flight response, which increases blood pressure, heart rate (HR), and respiratory rate. While this stressresponse mechanism is beneficial under acute stress, prolonged activation of the adrenergic system is thought to be detrimental to cardiac function and whole-body metabolism (22, 27). During the first 48 hours after burn injury, an increase in cardiac output, oxygen consumption, metabolic rate, and hyper metabolism characterize the “ebb phase.”These responses are thought to be driven by an elevation in catecholamines, which also disrupt insulin, glucose, lipid, and protein metabolism (42). The “flow” phase then follows within 5 days of burn injury to further disrupt metabolism (27).Much of the research on burn injury over the last 20+ years has centered oncharacterizing the hyper metabolic response and has greatly improved burn care (14, 27). In fact, due to these medical advances, patients with 90% total body surface area burns now survive these injuries; however, these improvements in burn care have resulted in children and adults with long-term metabolic and cardiovascular complications that persist for up to 3 years postburn (11, 14, 16, 40)and that are thought to be risk factors for long-term cardiovascular disease (9).

Cardiorespiratory fitness (peak VO_2) is a strong predictor of all-cause mortality (18). Beginning from5 years post burn until 10 or more years after the injury, adults have reduced aerobic exercise capacity (10, 41), suggesting thatlong-termcardiorespiratory impairments may be present. However, whether this is due to cardiovascular dysfunction or reduced physical activity post burn is not entirely clear(38).Additionally, burn trauma may affect children differently than adults, and this requires further study and understanding. Adult physiology may differ from that of children due to children's rapid growth and development during puberty coupled with morphologic differences (29).For example, children have a greater body surface area (BSA)-to-mass ratio and are less economical (use greater oxygen at similar exercise workloads) in regard to exercise compared to adults. Moreover, healthy non-burned children have smaller hearts, less blood volume, and lower stroke volume (SV)in response to exercise than adults (37).Reynolds and colleagues found that, in children, burn injury causes cardiac failure, particularly left ventricular myocardial depression, an outcome that was likewise different from that seen in burned adults(28).

Whether cardiovascular response to exercise is impaired in burned childrenis currently unknown. If this is the case, then rehabilitation exercise medicine may need specific guidelines for burned populations, especially if HR- or oxygen uptake-based training (i.e., percent HR/oxygen uptake max) is used as a guide for exercise prescription. Some have reported that burns do not affect children's exercise tolerance during a graded exercise stress test(20), while others have reported limited endurance exercise due to abnormal lung function at 2 to 3 years post burn (7, 21).

The objective of this study was to assess the cardiovascular response to submaximal exercise in childrennear1-yearpost burn (range: 7-15mo). We hypothesized that burn injury would attenuate cardiac output and SV during submaximal exercise in burned children compared to non-burned healthy children matched for age and aerobic capacity.

Methods

Ethical approval

All experiments were approved by the Institutional Review Board of the University of Texas Medical Branch and in agreement with the Declaration of Helsinki. Thirteen children participated in this study. Prior to participation in the study, informed consent was obtained from parents or legal guardians and child assent was obtained as applicable.

Experimental design

Upon admission to our institution, pediatric patients undergo standard of care treatment involving reconstructive surgery and skin grafting. They are then discharged once wounds are 95% healed. Patients return for follow-up at 6, 9, 12, and 24 months after discharge and yearly thereafter for further reconstructive surgery and continued care. This study was conducted in patients returning for the 9- to 12-monthfollow-up visits. Five burned children and 8 non-burned healthy children matched for age, height, weight, and exercise capacity participated in this study. Prior to the main study, an aerobic exercise stress test (peakVO_2) and body composition (dual-energy X-ray absorption metry [DXA]) scan were administered. Within 1 week of preliminary assessments, subjects participated in a submaximal exercise protocol that entailed a pre-exercise (pre-EX) standing rest period followed by 3-minute exercise stages at 20W and 50 W. During the rest and submaximal exercise, oxygen consumption, HR, cardiac output, SV, and arteriovenous oxygen difference were measured.

Peak aerobic exercise capacity test

Aerobic exercise capacity (peak VO_2) was determined by a modified Bruce protocol maximal treadmill exercise test to volitional exhaustion. Respiratory gasses were analyzed using breath-by-breath data using an automated Med Graphics CardiO_2 metabolic cart (St. Paul, MN) after O_2 and CO_2 gas and air flow were calibrated using known gasses and a 3 L syringe. Initial speed was set at 1.7 miles per hour and angle of elevation at 0%. These were then increased every 3 minutes. Subjects were continually encouraged to complete 3-minute stages, and the test was ended once peak volitional effort was achieved. Notably, no validated, universally accepted criteria exist in children for the determination of peak VO_2 [42]. Therefore, we used standards similar to those used in adults [27], and the test was deemed to be maximal once subjects signaled to stop exercise and at least 3 of the following criteria were met: a respiratory exchange ratio (RER) of ≥ 1.05, a leveling off in VO_2 with increasing workloads (less than 2 mlkgmin^{-1}), volitional fatigue, exercise final HR of 190 b pm or greater, or a final test time from 8 to 12 min. Similar criteria have been used by others in children [42,47]. All subjects met 3 of the aforementioned criteria.

Cardiac output and calculated stroke volume and arteriovenous difference

During the rest, while standing (pre-exercise), and during the two stages of submaximal exercise (20 W and 50 W), cardiac output and diffusing capacity (DLCO) was assessed using a non-rebreathing, open-circuitcardiac output (CO) and pulmonary diffusing capacity method previously described (17, 34). Briefly, the gas mixture consisted of 0.3% C^{18}O, 21% oxygen, 8% helium, 0.7% acetylene, and balance nitrogen (Scott Medical Products, PA). We

used a respiratory mass spectrometer (MGA1100, St. Louis, MO,) to sample gas at a mouthpiece attached to a screen-type pneumotachograph (3813 Hans Rudolph, Kansas City, MO).Athree-way pneumatic valve (8500 Hans Rudolph, Kansas City, MO) was used to switch the inhaled gas between room air and a 20 L bag containing the test gas mixture. During a CO maneuver, subjects inhaled from the bag and exhaled into the atmosphere. After 8 to 12 breaths, the respiratory valve was turned back to make inspiration from room air. Data analysis was performed immediately after each maneuver using a custom computer program that derived cardiac output from acetylene uptake while using gas dilution methods of the helium tracer gas to obtain alveolar volume. The dead space was calculated by gas dilution from helium for every maneuver. The pneumotachograph was calibrated using a 3 L syringe filled with test gas mixtures before each study. Stroke volume (SV, ml) was calculated as cardiac output divided by HR (beats per min), and arteriovenous O_2 difference ([a-v] $O_{2\ dif}$, ml/100 ml) was calculated as cardiac output divided by oxygen consumption (VO_2). According to Johnson et al. (2000) these methods in comparison to the direct Fick have a reproducibility of results where the coefficient of variation (%) were between 2.1% within sessions and 1.8% and the correlation to Fick is r^2=0.9.

Body morphology

Standard, calibrated scales were used to determine weight and height. Body composition (DXA, Hologic QDR 4500 densitometer, Hologic Inc., Bedford, MA)was measured within 7 days of the exercise protocol during the subject's first visit to the laboratory. On the day of each test, the DXA instrument was calibrated using the procedures provided by the manufacturer, and DXA scans were performed and analyzed using pediatric software. Three body mass indices were used: body mass index (BMI), BMI percentile (BMI% ile), and BSA. BMI (kgm^{-2}) was calculated by weight in kilograms divided by the square of height in meters. BMI % ile was determined using the normative values provided by the CDC (3), and BSA (m^2) was calculated according to the method of DuBois and DuBois (8). The burn patients in this study were admitted for flame (n=4) and scald (n=1) on the head, chest, back, arms or legs. Total body surface area burned and third-degree burn was calculated by nursing staff. At admission, total body surface area burned was documented in Lund and Browder charts and adjusted accordingly upon demarcation of third-degree burns.

Statisticalanalysis

Baseline subject characteristics were analyzed using an independent t-test. A two-way factorial ANOVA was used to assess the interaction and main effects of group × exercise. If significance was found, the appropriate Holm-Sidak multiple comparison *post hoc* test was performed. The rate of external work was calculated from the treadmill grade and speed using the following standard formula: W = body mass in kg × 9.81 × (speed in mph × 0.44704) × (%Grade /100). To control for growth and body morphology variations between burned and non-burned children, we normalized oxygen uptake (VO_2) and exercise work rate (Watts) to total body mass and lean body mass. Cardiac output and SV were also normalized to BSA. Slopes and intercepts for cardiac output, SV, HR, and arteriovenous difference were compared between burned and non-burned healthy controls. Data were analyzed and figures generated using Graph Pad Prism (Version 6.0, La Jolla, CA, USA), with significance set at P<0.05. All data are reported as mean ± SD.

Results

Subject characteristics

As shown in Table 1, the five burned children (2 female)had 49±4% total body surface area burns with 24.4% third-degree burns. They were comparable to the eight non-burned healthy controls (5 female) with regard to age (burn, 11.7±1 years vs. non-burned, 12.5±2 years), weight (burn, 40.4±18 vs. non-burn, 58.0±17 kg), and height (burn, 141.1±9 vs. non-burn, 147.3±12 cm) (P>0.05 for all). Burn children had a lower growth BMI-for-age percentile than non-burned controls (54.6±37 vs. 92.5±6 %tile; P=0.008). In burn patients, testing occurred at 9.4±3 mo post burn.

Peak and submaximal aerobic exercise

The burn and non-burn groups had similar peak VO_2 capacity relative to total and lean body mass as well as similar final RER and total exercise time (Table 1). However, absolute VO_2 was 42% less in the burned group (P<0.05). Additionally, burned children reached a peak exercise work rate (watts) that was 64% lower than that in non-burned healthy children (P<0.05). Burned children also had lower peak HR values (11% or 21 b pm decrease) than non-burned children (P<0.01).

Submaximal exercise was adequately matched between groups (Table 2). Absolute and total body mass- and lean body mass-normalized VO_2 and exercise work rate did not differ between groups for either of the two stages of exercise (group × exercise interaction, P>0.05). However, relative intensity (as a percentage of peak) for VO_2, HR, and work rate was different between groups. Burned children had greater relative oxygen cost, HR, and work rates than non-burned healthy children (group × exercise interaction, P<0.001).

The cardiovascular response to submaximal exercise is attenuated in burned children

Cardiac output in the burned group was reduced by ~28% at 20 W and 25% at50 W compared to the non-burned healthy group (group × exercise interaction, P=0.012) (Figure 1). SV did not differ from pre-exercise to 20 W and50 W in burned children. However, in the non-burned healthy group, SV increased from pre-exercise to 20 W by ~21% and from pre-exercise to50 W by 19%(main effect for exercise, P<0.05).Burned children also had an attenuated HR response compared to non-burned healthy children (group × exercise interaction, P<0.01). The arteriovenous difference increased to a similar degree in each group (main effect for exercise, P<0.01). When cardiac output and SV were normalized to BSA (Figure 2), the SV index was similar between groups; however, the cardiac output index remained lower in the burned group (group × exercise interaction, P<0.01).

The relationships between oxygen uptake and cardiac output, stroke volume, and arteriovenous oxygen difference are altered in burned children

The cardiac output slope strongly correlated with oxygen uptake in the non-burned group, whereas there was no significant relationship in the burned group (Figure 3A, r=.90, P<0.0001). Likewise, SV slope strongly correlated with VO_2 (r=.73, P<0.01), with no significant relationship being detected in the burned group. However, the slope for [a-v] $O_{2\ dif}$, and VO2 were strongly correlated (r=.72-.87) for both groups with significant slope

differences (P<0.01).We note that one non-burned individual was larger in body size than the remainder of the non burned group. When we removed this individual, Q (r=.43, P=0.008), and (a-v)O_2 (r=.47, P=0.005) remained strongly correlated; whereas SV did was not. In further analysis, we normalized to BSA to control for body size differences between burn and non-burned children and therefore kept this individual in the analysis.

Discussion

This study tested the hypothesis that burn trauma attenuates the cardiovascular response to submaximal exercise. We show, for the first time, that the cardiovascular response to submaximal exercise is weaker in burned children than innon-burned healthy children. Both cardiac output and SV were attenuated during submaximal exercise, with the former remaining reduced when normalized to BSA. Oxygen uptake and calculated arteriovenous difference were not different between groups. However, burn injury was associated with lower peak HR values during the peak VO_2 test along with a reduced HR and cardiac output response. These data suggest that cardiac dysfunction from burn injury may play a role in the impaired cardiovascular response to submaximal exercise in burned children.

It is worth mentioning that no established protocol exists for exercise testing in children. Children do not exhibit clear symptoms of fatigue that are supported by maximal HRs that level off at about 200, a RER>1.0, and a plateau in VO_2(1). Notably, this is due to children's development of cellular metabolic capacity (31). Because children generate less lactate and excess CO_2, an RER of 1.0 has been commonly used. However, we control for these by including only criteria established in adults and comparing groups with similar peakVO_2 characteristics (no difference in time to exhaustion, RER, or peakVO_2).Nevertheless, even though groups were matched for peak exercise capacity, peak work rate was significantly attenuated in the burned children. Additionally, we found for the first time that burned children have a significantly lower peak HR than non-burned healthy children.

Others have shown that adults assessed at 5 to 10 years post burn have a lower peak VO_2 and time to fatigue when compared to non-burned healthy adults (41) and published norms (10). In fact, Ganio et al. reported that 88% of the burned adult subjects studied had values below American Heart Associationage-adjusted normative values. Innon-burned adults, low cardiorespiratory fitness and aerobic exercise capacity (peak VO_2) are strong predictors of all-cause mortality (18),and burned adults with low aerobic fitness may be at greater risk of all-cause mortality relative to the general population. No standardized norms for children younger than 13 years old currently exist. Additionally, because both age and sex reportedly influence peak VO_2 in children, use of the ratio scale (i.e., kg total body mass) and absolute values may not be the best way to measure cardio respiratory fitness (2). However, according to normative data for non-burned healthy children aged 13 to 19 years available from The Cooper Institute for Aerobics Research, all of our burned children would fall into the very poor (<25 mlO_2·kg^{-1}·min^{-1})-to-poor (25-31ml O_2·kg^{-1}·min^{-1}) category (using standard ratio scaling) (15). In a review by Matecki et al., healthy non-trained boys and girls reportedly had a peak VO_2 of 47 ml O_2 kg min^{-1}and 40 ml O_2·kg·min^{-1}, respectively (19). Cooper et al. reported that healthy childrenaged 6 to 13years had aerobic capacities of 47 ml O_2·kg^{-1}·min^{-1}(4). We have reported in several other studies that at hospital discharge our

children with severe burn injuries have valuesin the range of 24 to 32 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$(12, 26).

Additional work from our institute has shown that metabolic and cardiovascular impairments are sustained for up to 3 years after burn injury (11, 14, 16, 40). How burn trauma affects cardiac function in humans is still not entirely clear. In animal models, burn trauma causes an increase in cardiac myocyte secretion of inflammatory cytokines (i.e., interleukin 1β, interleukin 6, and tumor necrosis factor α) coupled with an alteration in cardiac calcium homeostasis that is associated with impaired cardiac contraction and relaxation (32).There seems to be a parallel between the burn patients and patients with heart failure. A hallmark of heart failure is exercise intolerance, which is reportedly due to inadequate blood flow to active skeletal muscle secondary to impaired cardiac output (33, 43). We have also observed exercise intolerance in our children with severe burn injury (unpublished findings), and we have found that, exercising at 75% of their peak VO_2, burned children can complete only 20 min of exercise, while non-burned age-matched controls complete the full 30 min. These children report crying, nausea, and fatigue. Notably, we have previously shown that burned children have profound elevations in skin blood flow perfusion (40-60% of max) compared to non-burned controls (~10% of max)(30).Because of the hyper metabolic state and inability of damaged skin to regulate body temperature, issues that are similar to those seen in patients with heart failure may contribute to an impaired cardiovascular response to exercise due to the profound redistribution of blood to the peripheral skin; however, this is speculative and requires further understanding.

Notably, Reynolds et al. reported that, in children, burn injury causes cardiac failure, particularly left ventricular myocardial depression (28). In heart failure patients, there is a modest rise in SV (50-65ml) relative to that seen in healthy subjects (>100 ml). We observed a similar effect in our burn and non-burn groups. This attenuated increase in SV in heart failure populations is due to a blunted ability to increase both LV preload and ejection fraction (33, 43). Additionally, the heart failure literature suggests this is also due to a lower maximal heart rate, dilated left ventricle, and reduced resting left ventricular systolic function (25). Our analysis of burned children likewise revealed attenuated peak heart rate values during the peak exercise stress test, as seen by comparison to healthy controls. Most interesting patients with heart failure, the inability to increase left ventricular systolic emptying is due to an impaired intrinsic contractility, reduced(&F062)-adrenergic responsiveness, and peripheral arterial vasodilator response to exercise. Therefore it seems likely that the chronic sympathetic autonomic nervous activation induced by burn trauma may alter(&F062)-adrenergic responsiveness in cardiac muscle; however, this hypothesis requires further investigation.

Burn trauma also increases energy expenditure, and protein catabolism causes the loss of lean body mass and muscle wasting (13). Notably, in this study, we showed that burned children had a reduced growth BMI-for-age percentile compared to non-burned healthy children. In addition, burn patients are subjected to prolonged immobilization due to bed rest, which may cause deconditioning. In non-burned healthy adults, 14 to 60 days of sedentary bed restreduces SV and left ventricular mass (23, 39).Burn patients in the current study were hospitalized for 8-14 days. Therefore, it is not surprising that cardiovascular and

strength conditioning may reverse muscle wasting and physical capacity (12, 26). Thus, exercise training immediately after discharge is an important component of the standard of care in hospital settings because of its ability to restore lean body mass and exercise capacity (12, 26). Work from our laboratory has shown that a 12-week exercise program involving strength and aerobic exercise training has been shown to improve peak torque and peakVO_2 in conjunction with lean body mass (via improved fractional synthetic rate) (12). However, whether adaptations to exercise training also involve improvements in cardiovascular function in burned populations is currently unknown. Our study controlled for peak aerobic capacity and submaximal oxygen utilization (matched for both) and showed that when oxygen kinetics (VO_2 and [a-v]O_{2diff}) were similar, both cardiac output and SV were reduced during submaximal exercise in burned children (Figures1 and 3). This finding suggests that children with burn injury have impaired cardiovascular response and that exercise training may improve cardiovascular physiology, though this requires further study in burn patients.

Only a few others have investigated cardiac output and SV in response to submaximal exercise in healthy children using rebreathing cardiac output methods, and our data in non-burned healthy children are similar (36, 37). Cardiac physiology may differ between burned adults and children. Turley and Wilmore found that in non-burned healthy 7- to 9-year-olds, cardiac output and SV response to exercise differed from that in adults owing to smaller hearts and a smaller absolute amount of muscle doing any given work rate (37). Given that our burned group had significantly less age-sex BMI, this response may have been attributable to blunted growth from burn injury. However, as previously mentioned, because of the confounding effect of body size and growth in children with regard to exercise capacity and the use of standard ratio scaling, others have recommended that SV and cardiac output also be reported (i.e., to BSA)(5, 6). When we normalized both groups to BSA, cardiac output remained lower in burned children, further supporting the notion that burned children have impaired cardiovascular responses to submaximal exercise.

The relative intensity of exercise is commonly used for exercise prescription purposes in clinical populations (24). For adults, relative HR-based prescriptions are used for exercise training given the linear relationship between HR response and oxygen uptake during exercise. However, no validated approaches currently exist for children, and we have shown the percent peak HR, peakVO2, and peak exercise work rate significantly differs between burned and non-burned healthy children, a finding that requires further study. We have also shown that burned children have an attenuated peak HR compared to non-burned children, suggesting that formulas developed by others (35)to predict peak HR values for the purpose of estimating exercise intensity (percent peak HR) may not be a valid approach in burned populations.

In summary, we show that children with severe burns have a reduced cardiovascular response to submaximal exercise relative to non-burned healthy children. Further examination of the cardiovascular response to exercise in larger samples and the exercise training response for improving cardiovascular function have important implications for rehabilitation exercise medicine. In addition, understanding these responses will offer insight

into how to reduce long-term cardiovascular deficiencies and the risk of cardiovascular diseases in burned populations.

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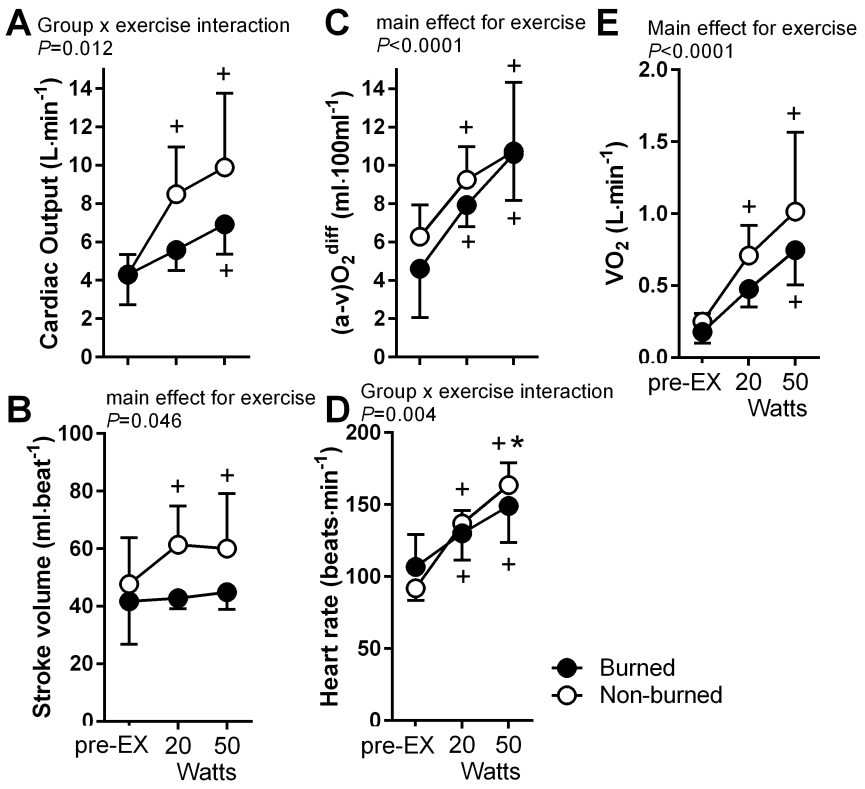

Figure 1.

Cardiac output (A), stroke volume (B), arterial-venous difference (C), heart rate (D), and oxygen consumption (E) during pre-exercise standing (pre-EX) and at 20 W and 50 W of exercise for burned (black filled circle; n=5) and non-burned children (open circle, n=8). *$P<0.05$ for burned vs. non-burned. $^{+}P<0.05$ vs. pre-EX.

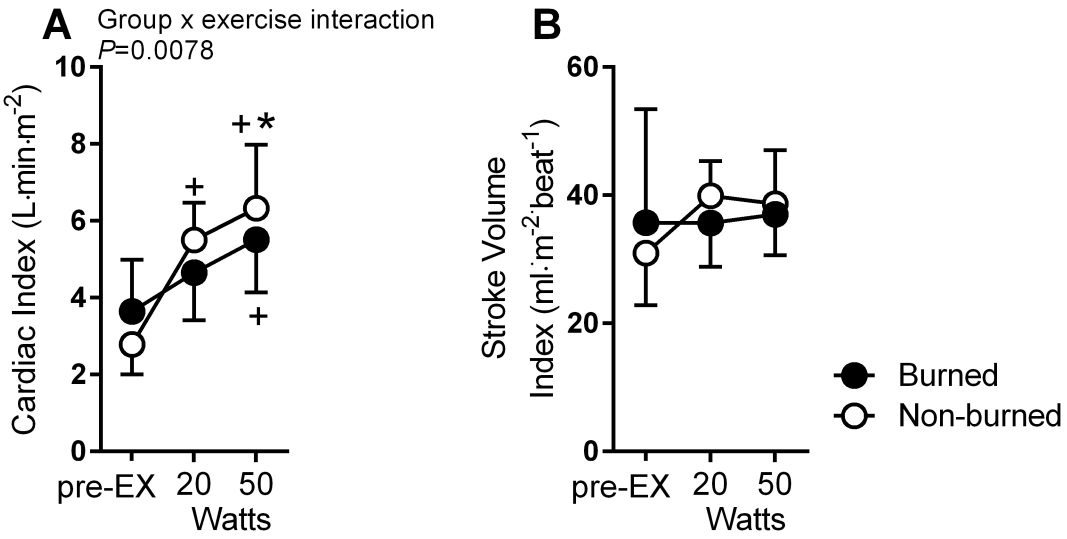

Figure 2.

Cardiac index (A) and stroke volume index (B) (normalized to body surface area) during pre-exercise (pre-EX) and at 20 W and 50 W of exercise for burned (black filled circle; n=5) and non-burned children (open circle, n=8). *P<0.05 for burned vs. non-burned. ^{+}P<0.05 vs. pre-EX.

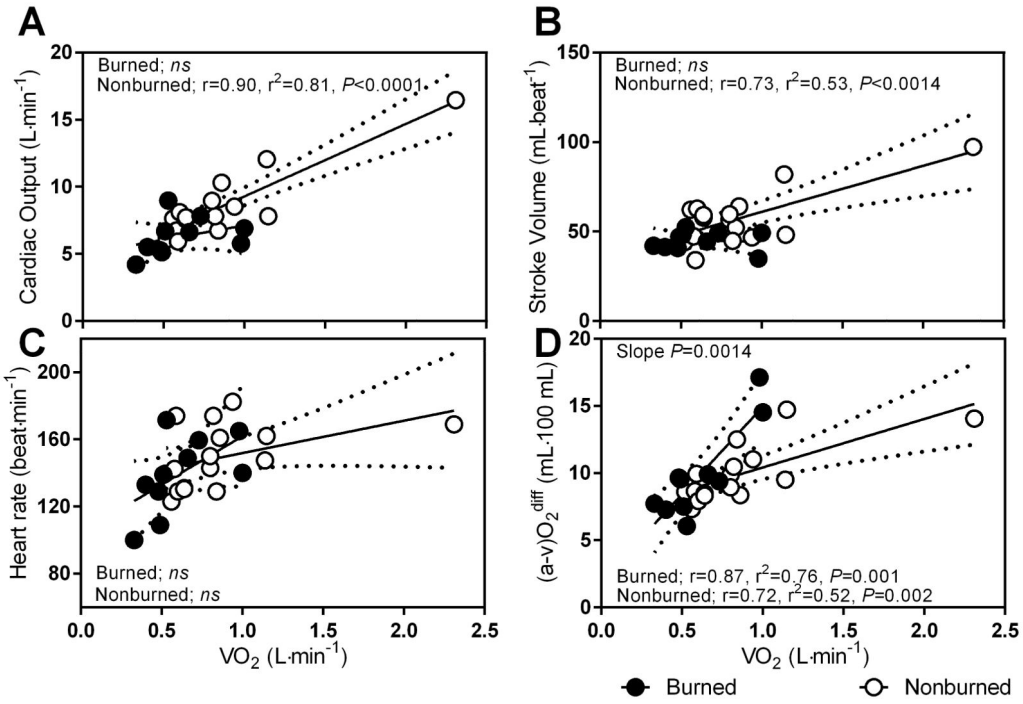

Figure 3.

Slope and intercept for cardiac output (A), stroke volume (B), heart rate (C), and arterial-venous difference ([a-v]O_2 ^{diff}) (D) during submaximal exercise for burned (black filled circle, n=5) and non-burned children (open circle, n=8).

Table 1
Subjects' physical and peak exercise characteristics (mean ± SD [range])

Characteristic	Burned	Non-Burned	*P* value
n (male/female)	5 (3/2)	8 (3/5)	-
Age (y)	11.7±1.4[10-13]	12.5±2.3[9-15]	0.50
Time of testing (months post burn)	9.4±3.4[7-15]	-	-
Length from admit to discharge (days)	13±3 [8-14]	-	-
Body Morphology			
Height (cm)	141.1±9.0[135-156]	147.3±12.3[123-162]	0.19
Weight (kg)	40.1±17.5[28-71]	58.0±16.8[31-71]	0.10
BSA (m^{-2})	1.2±0.3[1.0-1.7]	1.5±0.3[1.0-1.9]	0.09
BMI ($kg \cdot m^{-2}$)	19.7±5.5[15-20]	25.3±4.9[21-36]	0.08
BMI (%tile)	*54.6±36.6[13-98]	92.5±6.2[80-99]	0.01
Fat mass (kg)	11.5±10.2[5-41]	18.1±8.5[10-37]	0.44
Fat mass (% total body)	25.3±10.0[17-41]	30.5±7.2[27-41]	0.19
Lean mass (kg)	27.8±7.5[25-41]	39.1±11.5[21-59]	0.08
TBSA burn (%)	49.2±3.6[45-53]	-	-
TBSA 3rd-degree burn (%)	24.4±20.0[0-51]	-	-
Peak Aerobic Exercise			
Peak VO_2 ($L\ min^{-1}$)	*1.2±0.3[0.7-1.4]	2.1±0.7[1.3-3.6]	0.02
Peak VO_2 ($ml\ O_2\ kg^{TBM}\ min^{-1}$)	31.9±11.3[18-43]	36.8±8.4[31-51]	0.39
Peak VO_2 ($ml\ O_2\ kg^{LBM}\ min^{-1}$)	44.4±13.5[29-57]	53.7±7.3[44-62]	0.12
Respiratory exchange ratio (AU)	1.1±0.1[1.0-1.2]	1.1±0.1[1.0-1.3]	0.68
Exercise test time (min^{-1})	12.2±4.1[9-18]	13.6±2.4[11-18]	0.46
Peak HR ($beat\ min^{-1}$)	*175±16[152-195]	197±7[189-209]	0.01
Peak exercise work rate (W)	*101±79[27-125]	282±163[94-545]	0.04

BSA, body surface area; BMI, body mass index; BMI %ile, body mass index percentile for age; TBSA, total body surface area;VO_2, volume of oxygen; TBM, total body mass; LBM, lean body mass; HR, heart rate.

*Statistically different from non-burned healthy controls.

Table 2

Subjects' absolute and relative submaximal exercise characteristics

Exercise Characteristic	Burned		Non-Burned		*2-Way ANOVA*		
					Interaction	*Main Effect*	
	Exercise Stage 1	Exercise Stage 2	Exercise Stage 1	Exercise Stage 2	*Group × Exercise*	*Group*	*Exercise*
Absolute							
VO_2 (L min^{-1})	0.4±0.1	0.7±0.1	0.6±0.2	0.7±0.3	0.68	0.13	**0.008**
Exercise work rate (W)	13.3±11	43.3±31	23.3±25	57.2±26	0.83	0.35	**0.002**
Normalized (TBM, LBM)							
VO_2 (ml O_2kg^{TBM} min^{-1})	12.6±6	18.6±7	10.5±4	13.1±5	0.59	0.84	**0.007**
VO_2 (ml O_2kg^{LBM} min^{-1})	17.1±7	25.6±9	18.5±3	23.6±3	0.30	0.92	**<0.0001**
Exercise work rate (W kg^{TBM})	0.37±0.4	1.0±0.5	0.40±0.4	0.99±0.4	0.75	0.89	**<0.0001**
Exercise work rate (W kg^{LBM})	0.28±0.2	1.1±1.0	0.41±0.4	1.1±0.4	0.61	0.82	**0.003**
Relative Intensity (%peak)							
Peak VO_2 (%)	39±9	59±13 $^{+}$	32±8 *	41±11 $^{+}$	**0.002**	0.05	**<0.0001**
Peak HR (%)	74±9	85±9 $^{+}$	69±4 *	83±9 $^{+}$	**0.03**	0.40	**<0.0001**
Peak exercise work rate (%)	17±10	44±14 $^{+}$	12±16	26±19 $^{+}$	**0.008**	0.21	**<0.0001**

VO_2, volume of oxygen; TBM, total body mass; LBM, lean body mass; HR, heart rate.

* $P<0.05$ for burned vs. non-burned.

$^{+}$ $P<0.05$ for stage 1 vs. stage 2 exercise.

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