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Long-term effects of physical exercise during rehabilitation in patients with severe burns

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Abstract

Background—We have reported that a 12-week exercise program is beneficial for the exercise performance of severely burned children. However, it is not known whether the beneficial effects remain at 2 years post burn.

Methods—Severely burned children who received no long-term anabolic drugs were consented to this IRB-approved study. Patients were able to choose between a voluntary exercise program (EX-group) and no exercise (NoEX-group) after discharge from the acute burn unit. Peak torque per lean leg mass (PTLLM), maximal oxygen consumption (VO₂max) and percent predicted peak heart rate (%PPHR) were assessed. In addition, BMI percentile (BMI%) and lean body mass index (LBMI) were recorded. Both groups were compared for up to 2 years post burn using mixed multiple analysis of variance, and the level of significance was defined at $p < 0.05$.

Results—One hundred twenty-five patients with a mean age of 12 ± 4 years were analyzed. Demographics between the EX-group (N=82) and NoEX-group (N=43) were comparable. In the EX-group, PTLLM, %PPHR, and VO₂max increased significantly with exercise ($p < 0.01$). Between discharge and 12 and 24 months, BMI% increased significantly in the EX-Group ($p < 0.05$) but did not change in the NoEX-group. There were no significant differences between groups in BMI%, LBMI, PTLLM, and VO₂max at 24 months post burn.

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Authors' contributions

All authors made substantial contributions to the conception or design of the work (CDV, OES, CRA, PW, RPC) or to the acquisition, analysis, or interpretation of data for the work (DNH, OES, PW, LPK, RPM) and the drafting of the work or revising the intellectual content (all authors). All authors have approved the final version of the manuscript to be submitted.

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Conclusions—Exercise significantly improves physical performance of burned children. However, the benefits are limited to early time points and become greatly narrowed with further recovery time. Continued participation in exercise activities or a maintenance exercise program is recommended for exercise-induced adaptations to continue.

Keywords

burn; cardiopulmonary fitness; muscle strength; rehabilitation; exercise duration

1. Introduction

Over the past decades, advances in burn shock resuscitation, early burn eschar excision, and subsequent wound coverage have significantly reduced mortality in pediatric burns (1). Hence, patients with severe burns covering more than one-third of their total body surface are (TBSA) are expected to survive. The major contributor to the sometimes poor and in most cases late sequelae is the hypermetabolic response to burns, which is modulated by high serum levels of catecholamines, glucocorticoids, and proinflammatory cytokines (2). These acute inflammatory and endocrine responses are associated with a vast loss of lean body mass, muscle protein breakdown, and prolonged immobilization (3). Despite advances in burn care, these systemic responses are still present 2 years post burn and maybe beyond (4). As the number of burn survivors is increasing steadily, identification of long-term health problems is essential to determine the medical needs throughout post-burn rehabilitation.

Muscle endurance and cardiopulmonary fitness are essential components of health that need to be addressed in post-burn care, as well as during the early post-burn rehabilitation phase to reduce hypermetabolism and hasten social reintegration of burn survivors (5). To improve outcomes after severe thermal trauma, researchers have sought many new treatment approaches, including exercise in combination with long-term medications to reduce post-burn morbidity. However, there have been no investigations comparing participants in a voluntary post-burn exercise program with those not participating in any training for up to 2 years post burn. Hence, we compared long-term functional outcomes between pediatric burn survivors either participating or not participating in an exercise training program, in the absence of any long-term anabolic agents.

2. Methods

2.1. Patients and Care

Pediatric burn patients who were burned between 1997 and 2015 were consented to either and exercise program (EX-group) or no exercise (NoEX-group) in this IRB-approved study. Inclusion criteria included patients aged 7 to 18 years with healed burns covering 30% of their TBSA. Exclusion criteria included any of the following: leg amputation, anoxic brain injury, psychological disorder, quadriplegia, severe behavior or cognitive disorder, or receipt of an anabolic agent during acute hospital stay or after discharge from the acute hospital stay. Informed consent was obtained from the parent or legal guardian of the patient on the first day of admission to Shriners Hospitals for Children®—Galveston (Galveston, TX), and the physical rehabilitation program was initiated after discharge from the acute unit. For this

analysis, we included all pediatric burn patients who participated in a hospital-based post-burn exercise program at our institution regardless of the length of training. Initially, from 1997 to the end of 2008, patients were randomized to either a 12-week in-hospital physical rehabilitation program or a non-exercise control group. Starting in 2009, randomization was stopped, and participation in the exercise program was offered to all patients. However, all patients received standard medical care throughout their hospital admission and were offered standard follow-up care post discharge. Endpoints for body composition, muscle strength, and cardiopulmonary fitness were assessed at discharge from the acute unit, during the hospital-based exercise program (EX-group only), and at 12 and 24 months post burn.

The hospital-based exercise program was conducted as previously published by our group (6). Resistance and aerobic exercises were conducted under the supervision of an American College of Sports Medicine-certified exercise physiologist or trainer. Children underwent resistance training, which consisted of the following: bench press, leg press, shoulder press, biceps curl, leg curl, triceps curl, toe raises, and abdominal curls. Free weights or resistance machinery were used as applicable. During the first week of the exercise rehabilitation program, patients were instructed on proper weight lifting techniques and were educated on the use of the equipment. Weight loads were initially set at 50% of each patient's three-repetition maximum and were subsequently increased to attain the three-set of 12-15 repetition maximum between weeks 2 and 6 of training. During weeks 6 to 12, three sets of 8-12 repetitions were performed. In addition, aerobic exercise on a cycle ergometer or treadmill was performed three to five days a week, with each session lasting 20 to 45 minutes. No further strength training activities were allowed during the 12-week rehabilitation period, but normal activities and daily routines were encouraged.

2.2. Body Composition

Height, body mass, lean body mass, and lean leg mass of the dominant leg (kg) were assessed using dual energy X-ray absorptiometry (DEXA) with an instrument from Hologic (Waltham, MA, USA) as previously described by our group (7,8). Generated values were used to calculate lean body mass index (kg/m^2) defined as lean body mass (kg) / height (m)² and body mass index percentile (BMI%, %) based on the formula used by the Center for Disease Control and Prevention (9).

2.3. Muscle Strength

We prospectively assessed muscle strength as peak torque (Nm) and peak torque per body weight (%), examining the dominant leg using a Biodex Isokinetic Dynamometer (Shirley, NY, USA) as previously described by our group (7). Peak torque per leg lean mass (%) was also determined, being calculated as peak torque (Nm) / leg lean mass (kg) * 100.

2.4. Cardiopulmonary Fitness

Cardiopulmonary fitness was assessed using the maximal oxygen capacity ($\text{VO}_{2\text{max}}$, ml/kg/min), peak heart rate (beats per minute [bpm]), and resting heart rate (bpm). $\text{VO}_{2\text{max}}$ as well as peak and resting heart rate were measured using an Ultima CPX™ metabolic stress testing system and a Medgraphics CardioO2 combined O₂/ECG exercise system (St. Paul, MN, USA) as previously described (6,7).

2.5. Assessment of Endpoints in Healthy Unburned Children

Healthy unburned children were consented to determine normal ranges for BMI%, lean body mass index, peak torque per body weight, peak torque per leg lean mass, VO₂max, peak heart rate, and resting heart rate. Mean values plus standard error of the mean were then used to create shadowed areas in graphs displaying long-term follow-up data. In addition, these endpoints were obtained to assess if pediatric burn survivors could reach normal values at 2 years post burn.

2.6. Statistical Methods

Demographic variables were summarized with means and standard deviations for continuous data or counts and percentages for discrete data. Comparisons between treatment groups were performed by 2-sample Welch's t-test or chi-square test. For each outcome, a mixed multiple analysis of variance modeled the relation between the outcome and all combinations of treatment (EX-group vs. NoEX-group) and time (discharge, 12 months, and 24 months), adjusting for the potentially prognostic covariates sex, age, and TBSA burn, while blocking on subject to account for repeated measures. Differences among treatments and times were assessed by Tukey-adjusted contrasts. Further, since in some cases the treatment groups differed at discharge, contrasts were used to compare the changes between time points between both groups, with Hommel-adjusted p-values (10).

For the analysis of the two groups at the three time points, the data for each time point was selected as the nearest measure to that time point, allowing ± 30 days for the discharge time point and ± 90 days for the 12-month and 24-month time points.

For the subset of patients that exercised (EX-group) and had study endpoints assessed during the hospital-based exercise activity, a generalized additive mixed model (11) was used to model the association with each outcome due to time spent exercising since commencing the exercise program, adjusting for potentially prognostic covariates sex, age, TBSA burn, and time post discharge, while blocking on subject to account for repeated measures. In addition, for the NoEX-group, we set the start exercise date by randomly sampling (with replacement) time from discharge for the EX-group, and we set the end exercise date as 84 days later. A penalized regression spline accommodated any non-linear relation between the outcome and time spent exercising. In all statistical tests, the level of significance was accepted as $p < 0.05$, and analyses were performed using R statistical software version 3.2.1 (R Core Team, 2015, Vienna, Austria).

3. Results

3.1. Patient Demographics

One hundred twenty-five patients with a mean age of 12 ± 4 years were included in this analysis. Forty-three patients in the NoEX-group and 82 patients in the EX-group were studied. No significant differences were detected between groups in burn size, size of full-thickness burn, age, length of hospitalization, or sex (Table 1). Type of burn was also comparable between groups (Table 2).

3.2. Body Composition

BMI% was significantly lower in the EX-group than the NoEX-group at discharge ($p=0.04$) but similar at 12 months ($p=0.71$) and 24 months post burn ($p=0.34$, Table 3). A comparison of the change in BMI% from discharge to 12 and 24 months post burn revealed that the change in the EX-group was significantly greater than that in the NoEX-group ($p<0.05$ adjusted by Hommel). However, BMI% did not significantly vary with exercise duration (Figure 1).

In both groups, muscle mass, expressed as lean body mass index, significantly increased from discharge up to 12 and 24 months post burn ($p<0.05$). However, lean body mass index was similar in the EX-group and the NoEX-group at discharge ($p=0.07$), 12 months post burn ($p=0.96$), and 24 months post burn ($p=0.57$) (Table 3). Duration of exercise did not significantly affect lean body mass index ($p=0.37$) (Figure 2), with lean body mass index being unchanged in the NoEX-group during this time ($p=0.13$).

3.3. Muscle Strength

The peak torque per body weight values of the EX-group were comparable to the values of the NoEX-group at discharge ($p=0.95$), at 12 months ($p=0.93$), and at 24 months post burn ($p=0.39$). In both groups, peak torque per body weight improved significantly from discharge to 12 and 24 months post-burn ($p<0.01$, Table 3). Peak torque per body weight increased significantly with duration of hospital-based exercise ($p<0.01$), with no change being seen in the NoEx-group during this period ($p=0.53$) (Figure 3).

In both groups, peak torque per lean leg mass improved significantly from discharge to 12 months ($p<0.01$), and 24 months post burn ($p<0.01$, Table 3). Peak torque per lean leg mass increased significantly with duration of exercise ($p<0.01$, Figure 4). The NoEX-group showed a decrease in peak torque per lean leg mass during this time; however, it was not significant ($p=0.70$).

3.4. Cardiopulmonary Function

Over time, VO₂max increased significantly in both groups from to 12 months and 24 months post burn ($p<0.01$, Table 3). VO₂max increased significantly with duration of exercise ($p<0.01$), with the NoEX-group showing a non-significant decrease during this time ($p=0.17$, Figure 5).

Both groups showed comparable peak heart rate at discharge and at 12 months, and 24 months post burn (Table 3). However, peak heart rate increased significantly with duration of exercise ($p=0.01$, Figure 6). Peak heart rate remained stable in the NoEX-group during the same period ($p=0.61$).

Both groups had significantly different resting heart rate values at discharge ($p=0.03$) and at 24 months post burn ($p<0.01$, Table 3). However, resting heart rate was comparable at 12 months ($p=0.15$). Both groups showed comparable changes in resting heart rate over time at all follow-up appointments. Nevertheless, resting heart rate decreased significantly with exercise duration ($p=0.04$, Figure 7). No significant changes were seen in the NoEX-group during this period ($p=0.61$).

3.5. Assessment of Endpoints in Healthy Unburned Children

A total of 96 healthy unburned children (46 female, 50 male), with a mean age of 11 ± 3 years were studied. Measured values for body composition, muscle strength, and cardiopulmonary fitness are presented in Table 3.

4. Discussion

Our current study showed that muscle strength (Figures 3 and 4) and cardiopulmonary fitness (Figure 5 and 6) increased significantly due to hospital-based exercise. From discharge to 12 and 24 months post burn, BMI% increased significantly in the EX-group (Table 1). Interestingly, the lean body mass index was lower in the EX-group at discharge and caught up to values measured in the NoEX-group at the 1 year follow-up (Table 3). We found no significant exercise-related changes in the separately conducted analysis of BMI% and lean body mass index (Figures 1 to 2). At 12 months post burn, all exercise-related improvements had greatly narrowed, and for both groups, body composition and cardiopulmonary fitness measures had reached values comparable to those seen in healthy unburned children. At the 24-month follow-up, muscle strength and peak heart rate of pediatric burn patients were comparable to unburned children (Table 3).

Discharge BMI% assessments showed that pediatric burn patients have, on average, values below age-predicted values due to post-burn hypermetabolism. Patients in the EX-group exhibited significantly increased BMI% and LBMI from discharge up to 1 year post burn. In addition, BMI% changes were significantly higher in the EX-group than the NoEX-group. Given these findings, we can conclude that, along with post-burn exercise, close guidance and nutritional support during the rehabilitation process, as provided during a hospital-based exercise program, is able to improve body composition of pediatric burn survivors at 12 months post burn. Therefore, a hospital-based post-burn exercise program is perhaps able to counteract adverse consequences of burn-induced catabolism.

Faigenbaum et al.(12) conducted a review of the literature focusing on the duration of training-induced strength increases during youth resistance training and discussed the amount of training needed to maintain the improved strength. They stated that the current medical literature suggests that training-induced strength and power in children tend to rapidly regress back to untrained values as soon as the training is stopped. They further described that once-weekly maintenance exercise training could not maintain training-induced strength that had been gained through 20 weeks of resistance training in children (12). Another study in adolescent male baseball players showed that twice-weekly training is required to maintain strength gains attained through 12 weeks of resistance training (13). Thus, we postulate that a maintenance training program is required to preserve improvements in muscle strength and cardiopulmonary fitness achieved through the present exercise program. Aside from improving endpoints such as muscle strength and maximal oxygen capacity, exercise performed during childhood is beneficial for bone growth, psychosocial health, and prevention of obesity and cardiovascular diseases (12). Thus, exercise may provide additional benefits to children during the post-burn rehabilitation phase. A limitation of our current study is that we have not assessed psychosocial well-being or home-based exercise activities. Recent work from our institution showed that exercise

positively affects psychosocial outcomes (14). Here we describe data on only exercise performance or capacity, as this was the sole focus of the current study and our major interest. Nevertheless, the long-term assessment of physical activity (calories expected, number of steps taken, distances walked) as well as psychosocial activities in burn care are lacking and should be included in future exercise studies. Regardless, both groups were well matched, and we do not believe that home-based exercise activities, dietary habits, or psychosocial disorders biased long-term outcomes.

Recently, Nieuwenhuis et al.(15) reported findings related to long-term physiological outcome of pediatric burn survivors in the Netherlands. They studied a cohort of 24 burned children with burns ranging from 10 to 41% TBSA for up to 5 years post burn. They showed that muscular strength, aerobic capacity, and anthropometry did not significantly differ from age-predicted norms in pediatric burn survivors assessed between 6 months and 5 years post burn. However, these long-term results do not correlate with our findings. Our population of burn patients had burns that covered, on average, more than 50% of the TBSA (ranging from 30 to 92%). In addition, we compared our two study groups from discharge up to 24 months post burn. In contrast, Nieuwenhuis' group published follow-up measurements of smaller burns and compared them to age-predicted measurements. When comparing our results to age-predicted values, we were able to show that, regardless of the group, BMI% at the 24-month follow-up remains below 75%. Nevertheless, the current study showed that patients in the EX-group had significantly increased BMI, BMI%, and lean body mass index from discharge up to 1 year post burn. Furthermore, muscle strength and cardiopulmonary fitness improved significantly with the duration of exercise.

The beneficial effects of a hospital-based post-burn exercise program have already been described by our group for patients receiving a 12-week exercise program in combination with exogenous growth hormone (16) or oxandrolone (17). The goal of administering these anabolic substances is to enhance the benefits of post-burn exercise training by increasing lean body mass. However, patients receiving growth hormone alone or saline placebo injections, without an exercise program, showed significantly lower muscle strength than those groups who received saline or growth hormone with an exercise training program (16). It is important to point out that the current research is the first to assess the effect of any duration of hospital-based exercise program on physical and aerobic capacity in children who have received no anabolic agents during their post-burn rehabilitation. Thus, we were able to show that exercise alone has no significant effect on BMI, BMI%, or lean body mass index in our studied cohort. Nevertheless, changes in BMI% during the first year post burn were significantly higher in the EX-group than the NoEX-group ($P<0.01$). This leads us to conclude that post-burn exercise induces adaptations that help return BMI% to normal ranges.

The current study confirms previously published findings from our institution (7) that exercise training performed after discharge from the acute unit significantly increases muscle strength. Al-Mousawi et al. compared an exercise group to a no exercise group up to 9 months post-burn, whereas we studied our cohort up to 2 years post burn. In addition, we included varying lengths of hospital-based post-burn training programs in our analysis. We also included patients who trained for less or more than 12 weeks, which is the length of the

program we currently offer. During the first year post-burn, muscle strength and lean body mass of the EX-group increased significantly. Nevertheless, when looking farther beyond in the rehabilitation process, up to 2 years post-burn, we found that these beneficial effects of the exercise program diminished.

5. Conclusions

A hospital-based exercise program significantly improves muscle strength and cardiopulmonary fitness in severely burned children. Benefits of exercise during rehabilitation are visible for up to 1 year post burn but become greatly diminished at 24 months post burn. Continued participation in exercise activities or initiation of a maintenance exercise program is recommended so that exercise-induced adaptations can continue.

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Figure 1. Effect of exercise duration on body mass index percentile (BMI%). The model shows both the exercise (EX) and non-exercise (NoEX) groups, along with the 95% confidence interval (gray shading).

Figure 2.

Effect of exercise duration on lean body mass index (LBMI). The model shows both the exercise (EX) and non-exercise (NoEX) groups, along with the 95% confidence interval (gray shading).

Figure 3.

Effect of exercise duration on peak torque per body weight (PTBW). The model shows both the exercise (EX) and non-exercise (NoEX) groups, along with the 95% confidence interval (gray shading).

Figure 4.

Effect of exercise duration on peak torque per lean leg mass (PTLLM). The model shows both the exercise (EX) and non-exercise (NoEX) groups, along with the 95% confidence interval (gray shading).

Figure 5.

Effect of exercise duration on maximal oxygen consumption (VO2max). The model shows both the exercise (EX) and non-exercise (NoEX) groups, along with the 95% confidence interval (gray shading).

Figure 6.

Effect of exercise duration on peak heart rate (PHR). The model shows both the exercise (EX) and non-exercise (NoEX) groups, along with the 95% confidence interval (gray shading).

Figure 7. Effect of exercise duration on resting heart rate (RHR). The model shows both the exercise (EX) and non-exercise (NoEX) groups, along with the 95% confidence interval (gray shading).

Table 1

Characteristics of severely burned children.

	EX (n=82)	NoEX (n=43)	
	<i>Mean±SD</i>	<i>Mean±SD</i>	<i>p-value</i>
Age at burn, years	12±4	12±4	NS
female:male	23:59	9:34	NS
TBSA burn, %	56±15	54±14	NS
TBSA burn third, %	43±24	38±23	NS
Length of stay, days	38±30	33±22	NS

EX= exercise group, NoEx= no exercise group, NS= non-significant, SD= standard deviation, TBSA= total body surface area.

Table 2Type of thermal burns^{*} and limb amputations[#].

	NoEX (n=43)	EX (n=82)	
	<i>n</i> (%)	<i>n</i> (%)	<i>p-value</i>
Flame	37 (86)	68 (83)	NS
Electrical and flame	5 (12)	11 (13)	NS
Electrical	1 (2)	1 (1)	NS
Scald	0 (0)	2 (2)	NS
Limb amputations	7 (16)	15 (18)	NS

^{*} Determined at the time of admission.[#] Determined at the time of discharge from the acute unit. EX= exercise group, NoEx= no exercise group.

Long term outcomes of the exercise group (EX, n=82) and no exercise group (NoEX, n=43) & characteristics of healthy unburned children (HUC, n=96).

Table 3

	HUC	Discharge			12 months			24 months		
		EX	NoEX		EX	NoEX		EX	NoEX	
		Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM	Mean±SEM
BMI%, %	80±2	51±31	71±27		66±32	64±34		73±28	51±34	
LBMI, kg/m²	12±0	13±2	13.8±3		15±3	15±4		16±3	14.4±3	
PTBW, %	148±4	94±34	96±22		126±33	125±36		133±36	142.46	
PTLLM, %	1338±26	904±219	877±203		1177±204	1140±218		1151±308	1242±328	
VO2max, ml/kg/min	34±1	24±6	27±7		31±7	30±5		33±8	35±6	
PHR, bpm	183±3 [#]	181±16	178±14		183±16	176±19		186±14	184±14	
RHR, bpm	89±2 [#]	126±15	116±13		94±15	88±18		92±16	79±15	

[#] Assessed in 54 children. BMI%=body mass index percentile, LBMI= lean body mass index, PTBW=peak torque per body weight, PTLLM=peak torque per lean leg mass, VO2max=maximal oxygen capacity, PHR=peak heart rate, RHR=resting heart rate, SEM=standard error of mean