The Effects of a High Intensity Aerobic and Resistance Exercise Program on Lean Body Mass and Strength in Pediatric Victims with Severe Burn Injury

Kari A. Hultgren
Pacific University
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Abstract

Background

Severe burn injuries affect thousands of individuals each year, 30% of whom are individuals under the age of 16. The impact of severe burn injuries on physiological function is dramatic in survivors. It induces a surge of circulating pro-inflammatory cytokines, catecholamines, and glucocorticoids, which perpetuate a prolonged stress response that wreaks havoc in the body. This process often results in difficulty with functional abilities and a decreased quality of life for severe burn victims. Re-integration into society is quite difficult for this population, and they become at risk for long term health consequences. Generally, high intensity aerobic and resistance exercise therapy has proven to be beneficial in adults regarding lean body mass, strength, and cardiorespiratory endurance. Would these benefits carry over to pediatric burn patients?

Methods

An exhaustive medical literature search was performed using MEDLINE-Ovid, MEDLINE-PubMed, Google Scholar, Web of Science using the keywords: burn or burns, pediatric or children, and exercise. The references of these were reviewed for relevant studies. The included articles were assessed for quality utilizing the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE).

Results

Two articles met the eligibility criteria, both of which were randomized control trials. The two studies examined very similar primary and secondary outcomes, with the only major difference being the timeframe in which the pediatric burn patients began the exercise intervention. The results were very consistent between the two, both showing a significant improvement in strength and lean body mass. The overall quality of the original studies are moderate due to some limitations. Further studies can minimize these limitations and further elucidate what is known in regards to the effect of a high intensity aerobic and resistance exercise intervention in pediatric burn victims.

Conclusion

The studies examining the effect of an exercise program in addition to a standard rehabilitation program provide enough evidence to support its recommendation. However, further research is required to determine the extent of the effect of exercise in these patients and the most beneficial exercise regimen, in addition to how it affects direct measures of re-integration into society and long-term health outcomes.

KEYWORDS

Burns, children, and exercise

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The Effects of a High Intensity Aerobic and Resistance Exercise Program on Lean Body Mass and Strength in Pediatric Victims with Severe Burn Injury

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BIOGRAPHY

Kari Anna Hultgren was raised in Australia, but completed her bachelor's degree in Exercise Science from Bethel University, MN in 2012. She moved to Chicago in 2012 to complete her Masters in Applied Physiology at the University of Chicago Illinois, where she spent two years as a clinical research assistant in the Integrative Physiology lab, and as a teaching assistant in the Kinesiology department.
ABSTRACT

Background
Severe burn injuries affect thousands of individuals each year, 30% of whom are individuals under the age of 16. The impact of severe burn injuries on physiological function is dramatic in survivors. It induces a surge of circulating pro-inflammatory cytokines, catecholamines, and glucocorticoids, which perpetuate a prolonged stress response that wreaks havoc in the body. This process often results in difficulty with functional abilities and a decreased quality of life for severe burn victims. Re-integration into society is quite difficult for this population, and they become at risk for long term health consequences. Generally, high intensity aerobic and resistance exercise therapy has proven to be beneficial in adults regarding lean body mass, strength, and cardiorespiratory endurance. Would these benefits carry over to pediatric burn patients?

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Conclusion
The studies examining the effect of an exercise program in addition to a standard rehabilitation program provide enough evidence to support its recommendation. However, further research is required to determine the extent of the effect of exercise in these patients and the most beneficial exercise regimen, in addition to how it affects direct measures of re-integration into society and long-term health outcomes.

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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biography</td>
<td>2</td>
</tr>
<tr>
<td>Abstract</td>
<td>3</td>
</tr>
<tr>
<td>Table of Contents</td>
<td>4</td>
</tr>
<tr>
<td>List of Tables</td>
<td>5</td>
</tr>
<tr>
<td>List of Abbreviations</td>
<td>5</td>
</tr>
<tr>
<td>Background</td>
<td>6</td>
</tr>
<tr>
<td>Methods</td>
<td>8</td>
</tr>
<tr>
<td>Results</td>
<td>9</td>
</tr>
<tr>
<td>Discussion</td>
<td>15</td>
</tr>
<tr>
<td>Conclusion</td>
<td>19</td>
</tr>
<tr>
<td>References</td>
<td>21</td>
</tr>
<tr>
<td>Tables</td>
<td>22-23</td>
</tr>
</tbody>
</table>
LIST OF TABLES

Table I. GRADE Assessment: Characteristics of Reviewed Studies
Table II. Mean percent change in outcomes after 12 wk exercise intervention

LIST OF ABBREVIATIONS

BSA Burn surface area
DEXA Dual energy x-ray absorptiometry
LBM Lean body mass
OT Occupational therapist
PT Physical therapist
REE Resting energy expenditure
RET Rehabilitative exercise training
RM Repetition maximum
SOC Standard of care
VO_{2peak} Peak oxygen consumption
The Effects of a High Intensity Aerobic and Resistance Exercise Program on Lean Body Mass and Strength in Pediatric Victims with Severe Burn Injury

BACKGROUND

There are approximately 486,000 Americans each year who are admitted for burn treatment, 30% of whom are individuals under the age of 16. Fortunately, significant advances in medical care and treatment options have decreased the number of deaths each year related to burn injuries. However, the impact of severe burn injuries on physiological function in survivors is dramatic and affects both quality of life and functional abilities. This impedes the re-integration into society for numerous survivors and can result in long-term health consequences.

Severe burns (burns equal to or greater than 30% of total body surface area) have a significantly deleterious effect on the body, affecting multiple organ systems and wreaking havoc on the body’s normal physiological processes. A severe burn induces a surge of circulating proinflammatory cytokines, catecholamines, and glucocorticoids, which perpetuate a prolonged stress response.

There is a significantly higher demand for amino acids in this stressed state, causing the body to turn on its muscle mass as a source. Synthesis of acute phase proteins in the liver is heightened, as is synthesis of proteins for immune function and wound healing. In fact, the protein requirement in a severely burned individual may exceed 4 times that of normal. Consequently, there is a net breakdown of muscle protein to meet the accelerated demands. Unfortunately, this process is not easily reversed. Despite aggressive nutritional support, severe burn victims become cachectic and experience alterations in their metabolism of skeletal amino acids for years post trauma. This dilemma is hugely problematic, because a strong
association exists between depletion of muscle mass and survival. In fact, severe burn victims with reduced lean body mass have the lowest chance of survival.\textsuperscript{6}

The hallmarks of such a dramatic stress response include hypermetabolism, muscle wasting and severe muscle loss as a result of net muscle breakdown, and insulin resistance.\textsuperscript{4} The hypermetabolic effect of a burn injury can result in a persistent increase in resting energy expenditure from anywhere from 20-100\%, lasting from months to years.\textsuperscript{3}

The long-term consequences of these responses often include reduced cardiorespiratory capacity, muscle atrophy, insulin resistance, dyslipidemia, and glucose intolerance.\textsuperscript{6} Without intervention, victims may experience significantly reduced functional capacity, difficulty re-integrating into society, and an increased risk for diabetes and cardiovascular disease (CVD).\textsuperscript{7} In addition to the severe physiological changes that occur in adult burn victims, children may experience altered bone formation, disturbed growth patterns, psychosocial issues, and difficulties returning to school. Low work capacity and diminished muscle strength are two roadblocks that may severely influence these parameters.\textsuperscript{9} However, the prolonged morbidity that results in these pediatric victims may be mitigated by a number of interventions, namely exercise therapy.\textsuperscript{7}

Physical and occupational therapy and nutritional support are currently standard treatment for the functional recovery of a burn victim.\textsuperscript{9} Rehabilitation exercises are aimed at mitigating muscle deconditioning, and improving range of motion, contractures, and fatigue.\textsuperscript{10} However, researchers have found that muscle catabolism and weakness often persists after the standard 12-week rehabilitation
programs designed for burn victims. Exercise therapy has been proven to be significantly beneficial in patients with a number of chronic diseases, and there is evidence for the same to be true in adult burn victims. Exercise attenuates muscle catabolism and significantly improves lean body mass, muscle strength, and cardiorespiratory fitness. In addition, Paratz et al found that a high intensity exercise program significantly improved health related quality of life.

There is little existing data regarding the effect of cardiorespiratory and resistance exercise programs in the pediatric population. However, the studies that have been performed in pediatric burn victims have demonstrated significant benefits. Although there was initial concern that exercise programs may exacerbate the hypermetabolism that was already problematic in pediatric burn victims, there is strong evidence to support aerobic and resistive exercise as a therapeutic strategy for improving functional outcomes without a deleterious effect on metabolism. These additional studies indicate that this type of therapy could do far more good without causing harm to the patient.

A recent survey examining outpatient rehabilitation programs found that supervised aerobic and progressive resistance exercise training programs are not widely practiced in any population of burn victims. The need, therefore, to examine existing literature on the effect of cardiorespiratory and resistance exercise in burn victims is crucial, especially in the pediatric population.

**METHODS**

An exhaustive medical literature search was performed using Medline-OVID, Medline-PubMed, Google Scholar, and Web of Science using the keywords: burn or
burns, pediatric or children, and exercise. The references of these articles were reviewed for relevant articles. Studies were included if conducted on children ages 0-19 years with severe burn injuries, and if they evaluated the effect of cardiorespiratory and resistance exercise on LBM and strength. The included articles were assessed for quality utilizing the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE).14

RESULTS

The database search of Medline-OVID, Medline-PubMed, Google Scholar, and Web of Science produced a total of 107 articles to be reviewed. After reviewing these articles for relevance to exercise and pediatric burn injury, two randomized controlled articles met the inclusion criteria.

Hardee et al

This randomized controlled trial11 investigated the effect of a supervised, 12-week individualized exercise program on muscle mass, function, and mixed muscle fractional synthetic rate in children (n=24) in contrast to the 12-week standard of care in-hospital physiotherapy program (n=23) immediately upon discharge.4

Forty-seven children participated in the study. They had been admitted to Shriners Hospital for Children, Galvston, TX for acute burn treatment, and using the “rule of nines”, were assessed to have a BSA of >40%. Consent was obtained, and patients were subsequently randomly assigned to either the standard of care group (SOC) or the rehabilitative exercise-training group (RET). The method of randomization is not given. Both treatment groups received the standard of care physiotherapy program. This included an occupational or physical therapist twice
daily for 1 hour, and included positioning and splinting, range of motion and strengthening activities, and scar management techniques. However, the RET group additionally received individualized and supervised exercise training under a certified exercise physiologist. Each exercise session included resistance (bench press, leg press, shoulder press, leg extension, biceps curl, leg curl, triceps curl, and toe raises) and aerobic exercises (treadmill or cycle ergometer). Patients were familiarized with the equipment during the first session and instructed on proper weight lifting technique. The load started at 50-60% of 3 repetition maximum (RM) at the beginning and progressed to 80-85% of 3RM by the end of the program. Aerobic exercise included a 5-minute warm-up followed by 20-40 minutes on the treadmill or cycle ergometer at 70-85% of peak oxygen consumption ($\text{VO}_2$peak), 3-5 days per week.\textsuperscript{11}

The authors primarily examined whole-body lean body mass (LBM), function, and mixed muscle fractional synthetic rate. LBM was quantified by dual energy x-ray absorptiometry (DEXA) at discharge, post treatment, and 12 months post burn. Muscle strength and cardiorespiratory fitness were used to assess function. The Biodex System-3 Dynamometer was used to assess strength, and the modified Bruce protocol for treadmill exercise testing was used to assess $\text{VO}_2$peak. Poor mobility and incomplete wound closure prevented a functional assessment from being performed at baseline, so these measures were not assessed until after the 12-week intervention. Mixed muscle fractional synthetic rate was determined with five-hour stable isotope infusion studies in a subset of patients, followed by a muscle biopsy of the vastus lateralis and skeletal muscle analysis.\textsuperscript{11}
Results were analyzed using a repeated two-way ANOVA with Tukey post hoc correction for differences in height, weight, LBM, and muscle fractional synthetic rate, and unpaired Student’s t-test for patient characteristics, functional assessments, and the percentage change in LBM. Significance was set a P<0.05 for all analyses.11

The study groups were similar with regard to baseline characteristics. No significant differences existed between groups for height (both baseline and post treatment), body weight, sex, length of stay, and percentage of BSA. Body weight increased from discharge to post treatment, but there were no differences between treatment groups.11

An analysis of the functional testing demonstrated a significantly greater relative peak torque in the RET group compared to SOC (SOC, 106 ± 8.7 N·m mL·kg⁻min, kg, vs RET, 138 ± 8.6 mL·kg⁻min; P = 0.01). Cardiorespiratory fitness, as assessed via VO₂peak, was also significantly greater in the RET group (SOC, 28 ± 1.3 mL·kg⁻min, vs RET, 32.1 ± 1.3 mL·kg⁻min; P = 0.04). Collectively, these markers of functional ability are significantly higher in patients who undergo exercise training when compared to those in standard rehabilitation.11

Lean body mass also improved significantly in the RET group. While there were no changes in LBM between discharge and post treatment in the SOC group, the RET group demonstrated a significant increase in whole-body and regional LBM. A subsequent assessment and analysis was performed of LBM 12 months post burn injury to determine if early exercise training resulted in long-term muscle adaptations. The analysis demonstrated that the RET group continued to have a
significant percent change in whole-body and leg LBM (RET, 18% ± 3% and 31% ± 4%, respectively; P < 0.05).\textsuperscript{11}

Mixed muscle fractional synthetic rate was assessed in a subset of patients (SOC, n = 13; RET, n = 11). An analysis showed the there were no differences in muscle fractional synthetic rate at the time of discharge (SOC, 6.1% ± 1.4% per day, vs RET, 7.9% ± 1.7% per day). It declined significantly from discharge to post treatment (6.9% ± 1.1% per day to 3.4% ± 0.4% per day; main effect of time, P < 0.01), but this occurred in both groups and there were no differences in the magnitude of change from discharge to post treatment between groups (SOC, -2.9% ± 1.5% per day, vs RET, -4.3% ± 1.8% per day).\textsuperscript{11}

The authors note that a primary limitation of the study was failure to assess physical activity and nutrition during the intervention, as these factors have potential to affect the outcomes of the treatment. For example, the use of an accelerometer could have allowed the researchers to control for differences in physical activity.\textsuperscript{11}

Another limitation described by the authors is the study population. All participants came from the same burn center, and they were primarily of Hispanic nationality. Moving forward, the authors would like to see multicenter, randomized control trials where participants are not homogenous.\textsuperscript{11}

**Suman et al**

This randomized control trial\textsuperscript{9} examined the effects of a 12-week resistance program versus a standard rehabilitation program on muscle strength, LBM, and cardiovascular fitness in 35 pediatric burn victims. Unlike Hardee et al,\textsuperscript{11} who
examined the effect of an exercise program immediately upon discharge, Suman et al.\textsuperscript{9} waited to begin the intervention when participants were 6 months beyond discharge.

The study included 35 children, ages 7-17 years old who, according to the “rule of nines” were assessed to have >40% BSA. Patients were excluded from the study if they had one or more of the following: leg amputation, anoxic brain injury, psychological disorders, quadriplegia, or severe behavior or cognitive disorders. Informed consent was obtained during the first day of patient admission, after which each patient was randomized into one of two groups: the exercise-training group or the non-exercising group. The group allocations were 16 to the non-exercising group, which consisted of a standard 12-week, home-based physical rehabilitation program, and 19 to the exercise group, which received an individualized and supervised exercise training program in addition to standard medical care and treatment. Standard care, which both groups received, consisted of a 12-week conventional occupational therapy and physical therapy program twice daily for 1 hour. It is unknown whether the allocation process was blinded or concealed.\textsuperscript{9}

The researchers compared the effect of a resistance and aerobic based exercise program on muscle strength and lean body mass in contrast to the standard of care approach. All individuals randomized to the exercise group were sedentary prior to the intervention and had never participated in such a program before. Each exercise session included resistance (bench press, leg press, shoulder press, leg extension, biceps curl, leg curl, triceps curl, and toe raises) and aerobic exercises
(treadmill or cycle ergometer). Patients were familiarized with the equipment during the first session and instructed on proper weight lifting technique. The load started at 50-60% of 3RM at the beginning and progressed to 80-85% of 3RM by the end of the program. Aerobic exercise included a 5-minute warm-up followed by 20-40 minutes on the treadmill or cycle ergometer at 70%-85% of V02peak, 3-5 days per week. Patients were asked to refrain from strength-training activities outside of the supervised training sessions, but were permitted to continue normal daily activities.

The primary outcomes of the study were LBM, as measured by DEXA, and leg muscle strength, as measured by Cybex Norm dynamometer, which showed peak torque, total work, and average power using the Cybex software system. Each measurement was assessed both at the beginning of the 6- and 9-month periods. In addition, the authors examined resting energy expenditure (REE) pre and post intervention.

Results were analyzed by paired t-tests for within-group comparisons over time and by unpaired t-tests for between-group comparisons before and after the intervention. Significance was set a P<0.05 for all analyses.

The study groups were similar with regard to baseline characteristics. No differences existed between groups for height, body weight, age, body surface area, and percentage of BSA burned. Post intervention, both groups continued to be statistically similar with regard to age, height, and weight.

The analysis showed a significant post intervention increase in strength, as measured via peak torque, total work, and average power in the exercise group, but
not in the standard group (Table II). This occurred both with and without statistical normalization. In addition, the exercise group had a significant increase in LBM, which remained unchanged in the standard group. Segmental analysis of LBM showed a statistically significant increase in all areas except for arms in the exercise group. VO_{2peak}, which is a well-known marker for cardiovascular endurance and muscular ability to perform work, also increased significantly in the exercise group but not in the standard group (Table II). As already known, REE was elevated in both groups before the intervention. However, it remained unchanged in the exercise group but continued to increase significantly (15%) in the standard group.\(^9\)

The authors noted several limitations. Individuals from the exercise group and two from the standard group were unable to participate in the DXA scan due to missed appointments or technical difficulties, and their data is therefore missing.\(^9\) They also note that, while VO_{2peak}, strength, and LBM are measures of functionality and may represent the level of difficulty that a burn victim may experience in re-integrating into society, they are only surrogate measures. Suman et al\(^9\) recommend that more direct outcomes should be examined in future studies. Number of days to return to school or a psychosocial assessment, for example, would allow for a comparative look at re-integration into society between groups. This data could further strengthen the evidence for incorporating a high intensity exercise program into the rehabilitation program designed for a pediatric burn victim.\(^9\)

**DISCUSSION**

Hardee et al\(^{11}\) and Suman et al\(^9\) examined the effect of a high intensity aerobic and resistance exercise program primarily on LBM and strength in pediatric
burn victims, in addition to secondary outcomes such as REE and VO$_2$-peak. They examined the difference between a standard 12-week rehabilitation program involving an OT and PT twice daily, versus the standard program with the addition of a tailored and supervised exercise program involving high intensity aerobic exercise and resistance training.

Both studies showed a significant increase in strength, LBM, and VO$_2$-peak in the exercise groups, which likely occurred as a result of increased skeletal muscle to perform oxidative work.$^{9,11}$ Regarding lean mass, Porter et al$^7$ have found that the lean mass accrued in the exercise group was still maintained at 1 year after the injury.

The findings on metabolism differed slightly between the two studies. Suman et al$^9$ showed that an exercise program can actually prevent the dramatic and detrimental long-term increase in REE that occurs in burn victims. Hardee et al,$^{11}$ however, found the there were no differences in the basal fractional synthetic rate (similar to REE) between groups, which demonstrates that the exercise intervention did not negatively affect the hypermetabolism that occurs in burn victims. While follow-up research should be performed to more fully elucidate the effect of exercise training on energy expenditure in burn victims, the important finding is that exercise does not further worsen REE and therefore should not be a concern when prescribing exercise to pediatric burn patients. This was re-iterated in a study performed by Al-Mousawi et al.$^{12}$

Both studies did have some limitations, in addition to those pointed out by the authors themselves. In Hardee et al,$^{11}$ muscle strength and cardiorespiratory
fitness were not assessed until the end of the intervention, which prevents a pre and post comparison. It is unknown where the participants started on each of these parameters, so there is no context in which to compare the effect of the exercise intervention other than the standard group. Hardee et al.\(^\text{11}\) also examined muscle fractional synthetic rate, which demonstrates the anabolic effects of resistance exercise, and showed there were no differences at the time of discharge between groups. However, data was only obtained in a subset of their participants.

The blinding and allocation concealment processes were not discussed in either study, so neither of these factors is known. The investigators in both studies did not permit participants to engage in any strength training activities outside of the study. However, accelerometers were not utilized so it is unknown if participants were compliant with the instructions. Activity level outside of the study is a valuable piece of information to control for and should be considered in future studies.\(^\text{9,11}\)

Considering the difficulty that pediatric burn victims may experience in returning to school, future studies might examine whether increased strength, cardiovascular endurance, and LBM correlate with a faster return to school, and, whether psychosocial parameters are influenced. Future studies may consider incorporating markers of physiological function with direct measures of societal function. For example, while improved LBM is crucial to proper physiological function, is it correlated with improved quality of life and return to daily activities? Both studies examined the effect of exercise on physiological function, but there were no direct markers of an impact on quality of life, return to school, or activities
of daily living. While the impact of an exercise program on these factors was not the goal of the study, it could help demonstrate the power of a high intensity aerobic and resistance exercise program.

Though both studies had limitations, the research indicates promise for high intensity aerobic and resistance exercise to be utilized as standard of care therapy for pediatric burn victims. This intervention does not involve pharmaceuticals, risky side effects, and appears to be beneficial in all aspects. Considering exercise is utilized as a therapy for a number of acute and chronic conditions, and the benefits are incredibly well documented, it is surprising that a high intensity aerobic and resistance exercise program is not yet instituted as a standard of care for pediatric burn victims. While the details regarding the training regimen with the best outcome in this population are not yet known, it is known that exercise therapy is beneficial without detrimental outcomes.

Moving forward, the details of the most effective style of exercise intervention and timing are yet to be fully elucidated. Suman et al noted that despite improved muscle strength and power, the pediatric burn victims in their study still had persistent muscle weakness (as measured via absolute peak torque) when compared to children of similar weight, height, and age. The authors note that resistance training may cause an increase in muscle breakdown, known as exercise induced muscle damage, which can be measured via circulating creatine kinase. If this information is more clearly elucidated, it may affect the prescribed recovery time allotted for patients between workout sessions. The authors suggest that the 48-hour recovery period in their study may not have been enough time to allow for
muscle synthesis in this patient population. Further research is required to examine the effect of different rest intervals on creatine kinase and if a longer rest period has improved outcomes for muscle weakness.\(^6\)

Moreover, the sustained release of glucocorticoids and catecholamines that results from a severe burn injury causes hepatic, adipose tissue, and continued skeletal muscle dysfunction, which may lead to insulin resistance, dyslipidemia, and glucose intolerance.\(^4\) Considering the long-term implications from the metabolic dysfunction that occurs with severe burns\(^4\) it would be advisable to examine the effect of exercise on markers of inflammation and CVD, insulin resistance, and dyslipidemia in this patient population. Further mechanistic research is also indicated to more clearly delineate how exercise affects muscle synthesis and metabolism at the cellular level. This will provide better insight into how to best utilize exercise therapy in these patients.

**CONCLUSION**

While there is evidence that demonstrates significant benefits of exercise training on LBM and strength in pediatric burn victims, more research is needed to investigate other crucial outcomes, such as measurements regarding quality of life and time until return to normal activity. More data is also required to examine the effect of an exercise rehabilitation program over a standard program in regards to long-term health consequences of a burn injury, such as insulin resistance and CVD. Furthermore, it is unknown if pediatric burn victims who undergo a high intensity exercise program post injury have a decreased incidence of chronic diseases related to the burn injury down the road.
The results indicated by Suman et al\textsuperscript{9} and Hardee et al\textsuperscript{11} are overwhelming: the benefits of a high intensity aerobic and resistance exercise program in severely burned pediatric patients provide significant improvement in LBM and strength over standard treatment. Standard treatment can no longer be supported as a sole treatment strategy for this patient population, and it is imperative that clinicians be educated on the findings of these studies. With further research to clarify remaining questions in regards to this topic, it is hopeful that supervised and individualized high intensity aerobic and resistance exercise programs will become standard treatment for pediatric patients with severe burn injury.
REFERENCES

### Table I. GRADE Assessment: Characteristics of Reviewed Studies

<table>
<thead>
<tr>
<th>Design</th>
<th>Included Outcomes</th>
<th>Downgrade Criteria</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>Indirectness</td>
</tr>
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<td>Hardee et al(^11)</td>
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<td>Serious limitations(^a)</td>
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</tbody>
</table>

\(^a\) Lack of mention of blinding of the researchers who were collecting the data or allocation concealment

\(^b\) Lack of accounting for physical activity and nutrition

\(^c\) Confidence intervals not given but sample size seemed to result in a somewhat precise treatment effect
Table II. Mean percent change in outcomes after 12 wk exercise intervention

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<tr>
<th></th>
<th>Exercise Group (n = 19)</th>
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</tr>
</thead>
<tbody>
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<td>78.5% increase</td>
<td>2.10% increase</td>
</tr>
<tr>
<td>Average Power (Watts)</td>
<td>72.3% increase</td>
<td>8.3% increase</td>
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<tr>
<td>VO2peak</td>
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<td>1.35% increase</td>
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Data from Suman et al.⁹