ARTICLE

# The Role of Exercise in the Rehabilitation of Patients with Severe Burns

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PORTER, C., J.P. HARDEE, D.N. HERNDON, and O.E. SUMAN. The role of exercise in the rehabilitation of patients with severe burns. *Exerc. Sport Sci. Rev.*, Vol. 43, No. 1, pp. 34–40, 2015. *Severe burn trauma results in persistent skeletal muscle catabolism and prolonged immobilization. We hypothesize that structured rehabilitative exercise is a safe and efficacious strategy to restore lean body mass and physical function in burn victims. Here, we review the evidence for the utility of rehabilitative exercise training in restoring physiological function in burn survivors.* **Key Words:** burn injury, lean body mass, maximal oxygen uptake ($\dot{V}O_2$), muscle strength, skeletal muscle, rehabilitative exercise

## INTRODUCTION

Major burns (burns encompassing ≥30% of the total body surface area (TBSA)) are unique with regard to the prolonged and debilitating effect they have on multiple organ systems within the body (18,20) (Fig. 1). The resulting protracted morbidity reduces quality of life in burn survivors and impedes their return to society. Surviving a major burn marks the beginning of a long convalescence, where the restoration of normal physiological function is often not readily (if ever) achieved. Consequently, interventions including, but not limited to, surgery, pharmacological agents, diet, and exercise, all play important roles in the successful rehabilitation of the burn patient.

Exercise is generally considered to be a safe and efficacious approach to restoring physiological function in patients with various chronic diseases. However, inclusion of exercise regimens in the outpatient rehabilitation of patients who have undergone major trauma, such as a large burn, is not common (8), despite evidence demonstrating that exercise is an effective means of improving outcomes in this patient population (9). With this in mind, the purpose of this review article is to highlight the important role of exercise in the long-term rehabilitation of severely burned individuals by distilling current evidence regarding the effects of rehabilitative exercise in patients recovering from major burn trauma. Our central hypothesis is that rehabilitative exercise training (RET) after a major burn injury will restore lean body mass and physiological function at a greater rate and to a higher degree than conventional standard of care (SoC) rehabilitation (Fig. 2).

## THE PATHOPHYSIOLOGY OF MAJOR BURN TRAUMA

A surge of circulating proinflammatory cytokines, catecholamines, and glucocorticoids after burn trauma initiates a profound and sustained stress response unique to this type of trauma (20). Hypermetabolism (11), muscle wasting (15), and insulin resistance (20,21) are all hallmarks of the stress response to major burns. In particular, burn injury results in a 20% to 100% increase in predicted resting energy expenditure (11,20,35), which persists for months if not years after injury (8). This increase in energy expenditure can be managed to an extent by β blockade (17,19,35), occlusive wound dressings (3), and keeping patients in a warm environment (~32°C) (35). Despite these management strategies, increased metabolic rate still poses a considerable challenge in providing sufficient nutrition to this patient group. Indeed, in our hospital, patients are fed approximately 1.4 times their required caloric load as calculated by indirect calorimetry. Despite this abundance of calories and the provision of protein in excess of 2 $g \cdot kg^{-1} \cdot d^{-1}$, patients with major burns still become cachectic, with derangements in skeletal muscle amino acid metabolism persisting for years after trauma (15,27).

The fact that aggressive nutritional support cannot readily reverse catabolism in severely burned patients appears curious at first glance. However, this most likely reflects a heightened requirement for metabolic precursors elsewhere in the body that cannot be met by exogenous provision alone, at least acutely after trauma. Furthermore, although the cycling of carbohydrate and lipid stores in the body after burn trauma

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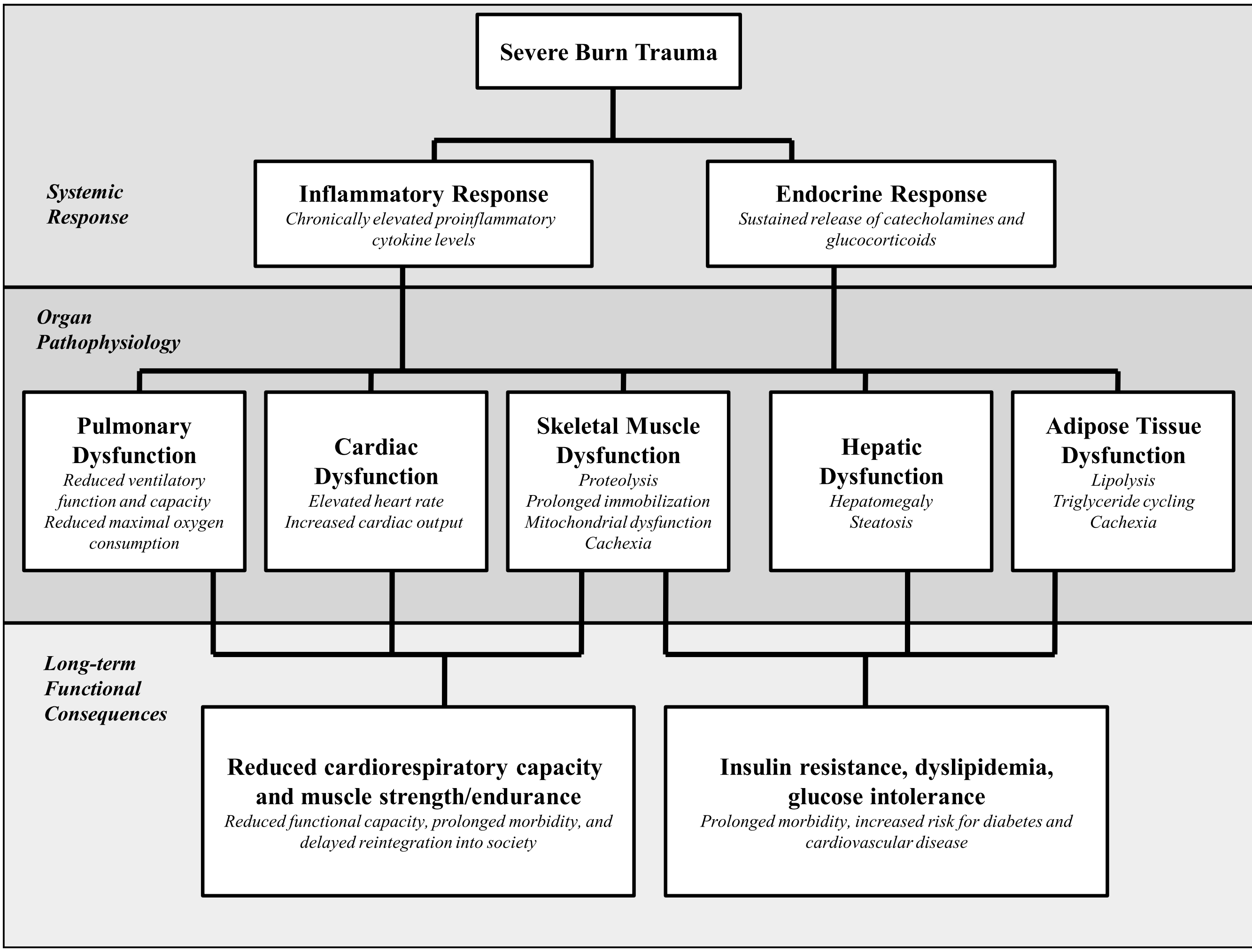


**Figure 1.** Schematic overview of the pathophysiological stress response to severe burn trauma. Chronic inflammatory and endocrine responses coupled with numerous surgical interventions and prolonged immobilization combine to cause profound metabolic dysfunction. Cachexia and deconditioning are synonymous with massive burn trauma and are leading contributors to the long-term functional impairment of burn victims.

significantly contributes to hypermetabolism (36), it is not without purpose. For example, the catabolism of adipose tissue triacylglycerol and muscle glycogen, most likely as a result of chronic adrenergic stimulation, provides the liver with glycerol and lactate, respectively, thus, facilitating the increase in *de novo* gluconeogenesis in response to burn trauma.

Although hypermetabolism (thermoregulation), muscle catabolism (acute-phase protein synthesis and wound healing), and altered substrate metabolism (endogenous glucose production) all play important roles in the acute response to burn trauma, these metabolic abnormalities often present long into patients' convalescence and contribute to the long-term morbidity of severely burned patients. Accordingly, strategies that mitigate these responses and restore normal physiological function likely will hasten the rehabilitation of patients with major burns.

## THE IMPACT OF REHABILITATIVE EXERCISE ON CARDIOPULMONARY FUNCTION

After major trauma, prolonged immobilization and the need for mechanical ventilation likely affect the pulmonary system. Burns, particularly flame-related burns, are often accompanied by inhalation injury. It is perhaps not surprising then that compromised pulmonary function is a component of the pathophysiology of major burns (7,13,33,34). Adults with severe burns have recently been shown to have impaired pulmonary function, as determined by spirometry, for up to 7 yr after injury (13). Furthermore, Willis *et al.* (34) reported that adults with severe burns have lower peak oxygen uptake ($\dot{V}O_2$ peak), have lower exercise tolerance, and participate in less physical activity than unburned controls. Interestingly, despite being approximately 5 yr postburn, three of the eight patients studied by Willis *et al.* (34) presented with either restrictive or obstructive pulmonary deficits. Thus, burn injury seems to be associated with altered pulmonary function, which likely impedes functional capacity. Consequently, restoring pulmonary function postburn likely will augment functional capacity.

The effect of exercise training on indices of exercise tolerance and pulmonary function in burn victims was first studied in children by our group. In a cohort of 31 severely burned children (aged 7–18 yr, >50% TBSA burns), $\dot{V}O_2$ peak at approximately 6 months after injury significantly was lower than that seen in aged-matched unburned children (31). Of

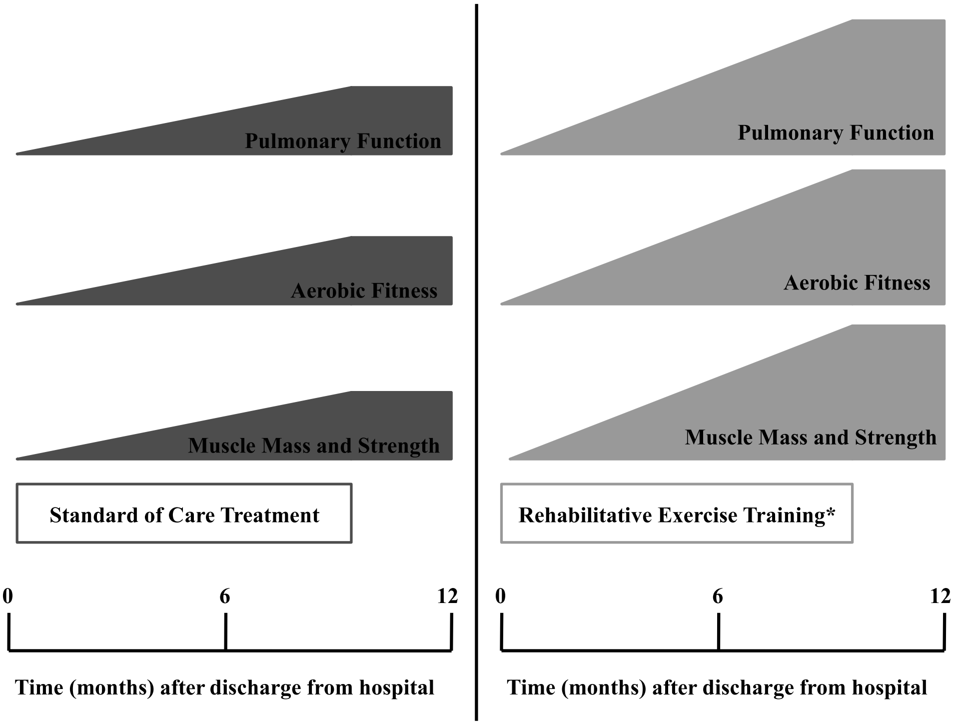


**Figure 2.** Conceptual illustration of the hypothesis that rehabilitative exercise training (RET) performed after hospital discharge results in a faster and greater restoration of lean mass and functional capacity in burn victims. *In our hospital, RET commences within 6 months of injury, is performed in an inpatient setting, and lasts for 6 to 12 wk depending on the extent of the patients' injuries.

these 31 burned children, 17 went on to participate in a 12-wk RET regimen (consisting of both aerobic and resistance exercise training). The remaining 14 patients served as time-matched controls and received standard outpatient burn care alone (SoC). $\dot{V}O_2$ peak significantly improved in the RET group, whereas no changes in $\dot{V}O_2$ peak were detected in the SoC group. More direct analysis of pulmonary function by means of spirometry revealed that maximal voluntary ventilation, forced vital capacity (FVC), and forced expiratory volume of air in the first second ($FEV_1$) were all significantly lower in burned children than in the unburned children. However, as with $\dot{V}O_2$ peak, maximal voluntary ventilation, FVC, and $FEV_1$ all significantly improved from baseline in the RET group but remained unchanged in the SoC group (31).

Our previous findings (31) contrast with those of a study conducted in a smaller cohort of burned adults ($n = 9$). In this study, pulmonary function, determined as the ratio of $FEV_1$ to FVC, was significantly lower in burn patients than in controls, but 12 wk of exercise training did not alter pulmonary function in either group, despite increasing $\dot{V}O_2$ peak (13). One reason for such a discrepancy may relate to the fact that Grisbrook *et al.* (13) determined the effect of RET on pulmonary function at an average postburn time of 6.6 yr, whereas Suman *et al.* (31) studied pediatric patients within the first year after injury. Indeed, baseline peak $\dot{V}O_2$ was not different between burned and unburned groups in the study by Grisbrook *et al.* (13), which in our view suggests that this patient group may have largely recovered its cardiorespiratory function by the time of the intervention. This suggests that the timing of exercise after injury may influence the magnitude of the response, particularly with regard to pulmonary function.

In a cohort of severely burned adults, de Lateur *et al.* (6) compared the effects of aerobic training and SoC treatment (control) on exercise performance. In this study, 35 adults with burns that required hospitalization (mean TBSA burned, 19%) were randomized to receive either SoC treatment or participate in a 12-wk aerobic exercise program, beginning on average 38 days post-burn and consisting of three treadmill sessions per week at an intensity of approximately 60% of heart rate reserve. Although control patients' aerobic capacity ($\dot{V}O_2$ max) marginally improved ($P > 0.05$), $\dot{V}O_{2max}$ significantly ($P < 0.05$) improved in patients who exercised (6), further suggesting that exercise improves functional restoration in burned adults to a greater degree than SoC treatment alone.

The implications of the aforementioned studies are severalfold. Reduced exercise capacity appears to persist for a number of years after burn injury and is associated with compromised pulmonary function. Consequently, it would be reasonable to conclude that impaired pulmonary function contributes to reduced exercise capacity in patients with major burns and that RET can restore cardiorespiratory fitness to some degree in severely burned patients. Thus, currently available data lend support to the importance of RET in the cardiorespiratory rehabilitation of patients with major burns.

## THE EFFECT OF REHABILITATIVE EXERCISE ON SKELETAL MUSCLE FUNCTION

Unloading of the skeleton is associated with skeletal muscle wasting. In addition to elevated catecholamine, cytokine, and glucocorticoid levels, and persistently elevated rates of

skeletal muscle proteolysis, burn victims also undergo prolonged immobilization after injury. Subsequently, patients with massive burns are severely cachectic (21). Insult to the musculoskeletal system after burn injury delays and limits patient rehabilitation, making strategies aimed at restoring muscle mass and function of paramount importance in the postacute care of burn victims. Indeed, adults with large burns have lower muscle peak torque and strength endurance than unburned individuals (10,29). What is most worrying about this finding is the fact that, in the study of St-Pierre *et al.* (29), patients had fully healed wounds and were studied at least 1 yr after discharge from the hospital (mean, 40.6 ± 26.3 months postburn). This demonstrates that the deleterious effect of severe burns on skeletal muscle function persists for many years after the injury.

Alloju *et al.* (2) showed that lean body mass (determined by dual-energy x-ray absorptiometry), isokinetic peak torque (determined by dynamometry), and muscle strength endurance (total work) were significantly lower in a cohort of 43 severely burned children (>50% TBSA burned) than in 46 unburned children. More specifically, peak torque and total work calculated during 10 maximal voluntary contractions of the quadriceps muscle group were 68% and 64% greater in unburned children than in burned children, respectively. Furthermore, burned children had 20% lower total lean body mass and 22% lower leg lean mass than unburned children (2). Not surprisingly, both peak torque and total work were significantly correlated with leg lean mass, underscoring the importance of restoring muscle mass in improving physical function in severely burned patients.

Previous work from our group has shown that severely burned children (>50% TBSA burned) participating in progressive resistive exercise for 12 wk, beginning at 6 months after injury, show improved upper and lower limb muscle strength relative to age-matched controls receiving SoC treatment alone (5). Furthermore, a 12-wk RET program incorporating resistance exercise (eight exercises focusing on compound movements involving the upper and lower limbs performed at 50%–80% of three repetition maximum), as well as aerobic conditioning (20–40 min at 70%–85% of $\dot{V}O_2$ peak three times weekly), has significant benefits for the convalescing burn victim (32). In this study, RET increased total lean body mass (trunk, leg, and arm) in children with large burns (>50% TBSA), whereas lean body mass was unchanged in a similar group of patients receiving SoC during the same time frame. Furthermore, isokinetic (150 degrees per second) peak torque and work capacity, as well as $\dot{V}O_2$ peak, increased in the RET group, with no changes being observed in the SoC group (32). Thus, RET had clear benefits on lean body mass and muscle function in children recovering from massive burns. Interestingly, whereas exercise likely resulted in transiently increased energy expenditure, RET did not worsen hypermetabolism in this patient cohort (32). Indeed, we have more recently reproduced this finding in similarly injured children, showing that RET, as compared with SoC, improves muscle mass and strength without worsening hypermetabolism (1). This underscores the safety and efficacy of RET in severely burned children.

Similar effects of exercise on skeletal muscle strength also have been seen in adults. In a cohort of 40 severely burned adults (>40% TBSA burned) studied approximately 6 months after injury, muscle peak torques of the leg extensors and flexors were 28% and 24% lower than those seen in a cohort of 23 unburned controls, respectively (10). Burned patients were randomized subsequently to one of two treatments: home-based exercise program focusing on range-of-motion exercises ($n$ = 20) or supervised isokinetic leg exercise three times per week for a total of 12 wk ($n$ = 20). In the group receiving supervised isokinetic exercise, leg extensor and flexor peak torques significantly increased to values that were similar in magnitude to those of unburned controls, whereas no significant improvements were detected in the group randomized to home-based exercise (10). Therefore, it would seem that supervised exercise interventions are significantly more efficacious in restoring skeletal muscle strength than home-based programs. This underscores the importance of including individualized supervised RET as part of outpatient care, particularly when RET can be performed in a hospital/clinic setting.

The utility of combined resistive and aerobic exercise training in restoring function in severely burned adults was further demonstrated by Paratz *et al.* (24). These researchers showed that, after wound healing, patients who participated in an exercise program consisting of three weekly hour-long sessions of aerobic and resistance exercise significantly increased their muscle strength and exercise performance (shuttle test) compared with baseline and compared with a group of patients who did not take part in any exercise program postburn. A novel aspect of this study was that RET was also associated with improved quality of life, suggesting that the benefits of exercise training after burn injury are not limited to physiological parameters.

With the existence of vast skin wounds encompassing one or more joints of the body, as well as muscle wasting so severe that wasting of one muscle in an antagonist muscle pair creates chronically flexed joints, burn patients typically require numerous corrective surgeries long into convalescence. In addition to improving measures of functional capacity, RET has been shown to reduce the number of surgeries required at 12, 18, and 24 months after injury in severely burned children when compared with SoC rehabilitation (4). Furthermore, RET has also been shown to reduce the amount of contracture releases required in severely burned adults (24). Although RET increases muscle mass and strength in burn victims, the effect of exercise on joint mobility and range of motion likely contributes to the reduced number of corrective surgical procedures required in patients who participated in RET after injury. Indeed, children younger than 7 yr who receive exercise and music therapy in conjunction with physiotherapy have better passive and active range of motion of the knee and elbow than patients who receive physiotherapy alone (23), further suggesting that RET also may prevent joint contractures.

## EVIDENCE FOR THE USE OF RET IN COMBINATION WITH PHARMACOTHERAPY IN THE REHABILITATION OF BURN

A number of pharmacological agents have been shown to mitigate the pathophysiological stress response to thermal trauma. In the acute period after injury, $\beta$ blockade with

propranolol lessens tachycardia, hypermetabolism, and muscle catabolism in children with major burns (19). These effects can be maintained with long-term propranolol treatment (12 months), improving growth and body composition in burned children (17). We recently published data concerning the effect of long-term propranolol treatment and RET versus RET alone in children with major burns (25). In agreement with previous findings, RET significantly increased lean body mass and peak torque, where the magnitude of improvement in these outcomes was similar in patients treated with RET and RET + propranolol. However, with regard to $\dot{V}O_2$ peak, the 22% improvement from baseline seen in the RET group, although a significant within-group change, was significantly lower than the improvement (36%) in $\dot{V}O_2$ peak observed in the RET + propranolol group (25). Although a mechanistic explanation as to why propranolol and exercise have an additive effect on $\dot{V}O_2$ peak in burned children is currently lacking, the ability of propranolol to attenuate peripheral protein catabolism and blood flow (12) may contribute to improved muscle mass and quality as well as $O_2$ extraction from arterial blood. However, it is important to note that, although $\beta$ blockade is associated with detriments in muscle function in healthy adults (22), this is not the case in severely burned children.

Because burn injury results in persistent muscle wasting (15), testosterone analogs have been used in burn victims to improve skeletal muscle amino acid retention. Oxandrolone has been studied in detail in our hospital in recent years because of its low incidence of androgenic side effects when compared with other similar agents. Hart *et al.* (16) demonstrated that, in the acute period postburn, oxandrolone treatment increases skeletal muscle protein synthesis, resulting in a more favorable balance between protein accrual and protein loss. More recently, Porro *et al.* (26) demonstrated the efficacy and safety of long-term oxandrolone treatment in burned children, showing that hypermetabolism is attenuated and that growth, lean body mass, and bone mineral content are all greater in oxandrolone-treated patients than in controls.

In our hospital, Przkora *et al.* (28) compared cohorts of patients who had received SoC ($n$ = 11), RET ($n$ = 17), long-term oxandrolone treatment ($n$ = 9), or both RET and long-term oxandrolone ($n$ = 14). Patients were randomized to receive either placebo or oxandrolone at hospital discharge. Exercise testing and body composition measurements were made at 6 and 9 months postburn, with RET being carried out in the 12 intervening weeks. Muscle strength (peak torque) significantly increased from baseline in all groups except SoC, with no additive effect of RET and oxandrolone being seen. Lean body mass also changed significantly in all groups, with the exception of the SoC group. However, in this instance, the percent change in lean mass significantly was greater in the RET + oxandrolone group than in either the RET- or oxandrolone-alone groups. Lastly, $\dot{V}O_2$ peak only increased in the two groups that participated in RET (28).

The aforementioned study suggests that both RET and oxandrolone can increase lean body mass in severely burned children, with there being an apparent additive effect of RET and oxandrolone treatment. However, although oxandrolone treatment alone increased peak torque to a similar degree as both the RET and RET + oxandrolone, improvement in $\dot{V}O_2$ peak seemed to be independent of oxandrolone treatment and dependent on RET. Thus, combined therapy with RET and oxandrolone can augment improvements in lean mass in burned children, but improvements in muscle function associated with RET are only partially mimicked by oxandrolone treatment alone. This evidence suggests that a combination of oxandrolone and RET better restores lean body mass and muscle function than either RET or oxandrolone treatment alone.

Using a design similar to that of the aforementioned study (28), we have investigated the independent and combined effects of RET and growth hormone treatment in the rehabilitation of severely burned children (30). Patients were randomized to receive either recombinant human growth hormone ($n$ = 20) or placebo ($n$ = 24) after discharge from the hospital. Within the growth hormone group, 10 patients received RET and 10 received SoC. Within the placebo group, 13 received RET and 11 received SoC. Testing was conducted at 6 and 9 months after injury (before and after RET) in both the RET and SoC cohorts (30). Lean body mass significantly increased to a similar degree in all groups except the SoC group. Thus, growth hormone treatment and exercise improved lean body mass but, unlike oxandrolone, growth hormone had no additive effect with RET. Both peak torque and $\dot{V}O_{2peak}$ increased to similar degrees in the RET and growth hormone + RET groups, meaning that exercise-induced improvements in muscle function were independent of exogenous growth hormone provision.

Currently, it would seem that many drugs have the potential to impact lean body mass in burn victims positively. Interestingly though, exercise alone also improves lean body mass to a similar degree as both oxandrolone and growth hormone, highlighting the importance of RET in restoring lean body mass in burn victims. With that said, a combination of drug therapy and RET may have additive effects for some, but not all, outcome measures. What seems to be a consistent finding, though, is that RET is a prerequisite for improved muscle mass and function, pointing to the value of this approach in improving functional capacity in severely burned patients.

## PRACTICAL CONSIDERATIONS

Typically, the metabolic derangements accompanying burn trauma become more pronounced when the TBSA afflicted reaches 20% to 30%. Indeed, we and others have shown that adrenergic stress and hypermetabolism become particularly ardent when burn lesions encompass 40% or more of the TBSA (34). With that said, comorbidities such as inhalation injury, blunt trauma, orthopedic complications, and sepsis likely worsen aspects of the stress response to burn trauma; thus, smaller burns with comorbidities may incur a similar metabolic insult as a large burn alone. Clearly then, outpatient care needs of burn survivors should not be decided arbitrarily by TBSA alone because a number of factors, including but not limited to, TBSA burned, length of stay in the intensive care unit, sepsis, inhalation injury, and time immobilized will influence a patient's need for long-term outpatient care. Broadly speaking, at our institute, patients with less than 60% TBSA burn perform 6 wk of RET after discharge from the hospital, whereas those with

burns encompassing more than 60% of TBSA participate in a 12-wk RET program because of their greater clinical complications. However, we advocate a highly personalized approach, dependent on the patients' particular clinical complications and rehabilitative needs.

Victims of large burns are undoubtedly one of the most challenging patient groups with regard to prescription of RET. Burns encompassing 50% or more of the body likely involve lesions that cover one or more of the body's major joints and depending on the severity/depth of the burn, may require amputation of digits and even entire limbs. Therefore, burned individuals are unique with regard to their need for highly personalized RET programs. Our institution houses a dedicated wellness center, which caters specifically to severely burned children. The availability of such a facility, with its specialized equipment and exercise physiologist/trainers experienced in training severely burned pediatric patients, is vital to successfully performing RET in burn victims. Furthermore, an in-house facility allows patients to perform RET immediately after discharge from the acute care unit as outpatients. This likely increases adherence to RET programs, where patients attend exercise session appointments as outpatients, much like attending clinic appointments for occupational/physical therapy.

The optimal time for initiating RET in burn patients has received little attention thus far. In general, from reviewing the literature, it seems that a conservative approach has been taken until recently, where RET programs have been initiated approximately 1 yr postburn (10,13), when burn wounds are fully closed and the worst of the pathophysiological response has subsided. In our hospital, patients were typically randomized to receive either SoC or RET to test the efficacy of RET on functional outcomes in burned children (1,4,5,25,28,30–32). In these instances, RET was performed at 6 months postburn, when patients return to the hospital for follow-up treatment. Given the positive effects of RET on aerobic fitness and muscle mass and strength, we no longer believe that it is ethical to randomize patients to SoC or RET. Because of this, we now offer all patients the option of staying at our hospital and participating in RET. To make this more feasible, we offer RET as part of the standard rehabilitation program that patients undergo after discharge from the acute care unit (typically 1–3 months postburn depending on injury characteristics). Indeed, we recently have published data from a cohort of patients who performed RET immediately after discharge from the hospital. We were able to show that RET initiated at this early time point after injury resulted in greater accrual of lean mass than SoC. Furthermore, aerobic fitness and strength were greater in the RET group than the SoC group at 6 months postburn (14). The greater accrual of lean body mass was maintained in the RET group at 12 months after injury, suggesting that alterations in body composition achieved through early RET are maintained at 1 yr postburn.

Although we believe that patients remaining in-hospital for RET is ideal, we acknowledge that this is not always feasible. We have used this strategy successfully in pediatric patients coming from Central/South America for treatment, making it somewhat easier for patients and their families to remain at our institution for RET. However, this may not always be the most practical solution, particularly for adult patients who have jobs and family commitments nearby, which may limit a prolonged hospital stay. In this instance, we advocate the prescription of outpatient RET in an exercise facility near the patient's residence. A benefit of such an approach is that patients can stay at home during the RET program while beginning to reintegrate into their pre-injury life. A limitation of this approach is that the specialized equipment and staff needed to train severely burned individuals are not always readily available in the community setting. Furthermore, whether or not health care providers will fund RET for burn victims may limit availability of this therapy.

## SUMMARY REMARKS

Major burn trauma is unique in terms of the long-term deleterious effects it inflicts on numerous physiological systems within the body. The pathophysiological stress response accompanying burn injury persists for several years (21), as do detriments in functional capacity (25). Thus, given that i) burn injury results in major impairments in physical function and ii) advances in acute clinical care mean that major burns are more survivable than ever before, there is a real need for effective rehabilitative strategies that augment functional capacity in burn survivors. In our view, empirical evidence clearly demonstrates that RET improves measures of physiological function such as aerobic capacity and strength in patients recovering from severe burns. For this reason, progressive RET should be a component of the outpatient care of burn survivors. Given that RET is not standard outpatient care in many burn hospitals, there is a need to increase awareness of the efficacy of RET in improving outcomes of burn survivors among care providers and institutes. Future research efforts should focus on identifying specific exercise modalities and RET regimens that confer the greatest improvements in physical function.

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