

AWARD NUMBER: W81XWH-14-2-0160

TITLE: Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health, and Physical Performance

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REPORT DATE: SEP 2020

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE (DD-MM-YYYY) Sept 2020		2. REPORT TYPE Final		3. DATES COVERED (From - To) 09/15/2014 - 06/14/2020	
4. TITLE AND SUBTITLE Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health, and Physical Performance				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-14-2-0160	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Oscar E. Suman, PhD Professor, Department of Surgery The University of Texas Medical Branch at Galveston Email: oesuman@utmb.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) The University of Texas Medical Branch 301 University Boulevard Galveston, Texas 77555-0156				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, MD 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S) USAMRDC	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT Prolonged inactivity accompanying stays in the burn intensive care unit (BICU) and hospital worsen muscle loss/weakness and lengthen hospitalization. We hypothesized that a personalized, structured, and quantifiable exercise program (MP10) would improve these variables over standard-of-care (SOC), as exercise has well documented effects on maintaining/improving muscle strength, which should shorten hospitalization. Thus, we characterized: (Aim 1) what was the SOC throughout hospital stay across the US and (Aim 2) we characterized the outcomes in burn in-patients. Over 4 years, we enrolled 77 patients aged 7-60 years with ≥30% TBSA burns. MP10 began ~4-5 days after the first surgery after admit (or most importantly, when the burn surgeon deemed mobilization safe) and continued for the entire BICU and hospital stay. MP10 took place on weekdays in the morning and afternoon. In the morning, patients participated in a 10-minute leg-crank ergometry session (Monark leg ergometer), starting with a load (watts) eliciting a 3-5 rating on the Borg Rated Perceived Exertion (RPE) scale. The number of revolutions in 10 minutes and minute-by-minute muscle and respiratory effort RPE was noted. In the afternoon, patients participated in a 10-minute arm crank ergometry session, which was done similarly to lower body exercise. Endpoints were lean mass, cardiopulmonary and muscle endurance, length of BICU, ventilator and hospital stay, and measures of Quality of Life. Within- and between-group comparisons were performed. MP10 was safe and can be added to standard of care in the ICU. It can also be a platform for future rehabilitation programs.					
15. SUBJECT TERMS Exercise, burns, standard of care, MP10, early exercise, lean mass, muscle strength, 6-minute walk					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT Unclassified	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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1. INTRODUCTION:

The title of this project was “Early Exercise in the Burn Intensive Care Unit Decreases Hospital Stay, Improves Mental Health and Physical Performance”. It had four sites: The University of Texas Medical Branch = UTMB-Galveston, TX; the United States Army Institute for Surgical Research = USAISR-San Antonio, TX; the University of Texas at Southwestern = UTSW-Dallas, TX; the University of California at Davis = UC-Davis. The prolonged inactivity that occurs in the burn intensive care unit (BICU) and hospital, results in worsening of muscle loss, muscle weakness, and in increased BICU and hospital stay. We needed to reduce this time to speed up resuming normal physical activities, returning to work or to professional duties. To this end, we had two aims: **Aim 1**: was to characterize, via a survey(s) the Standard of Care of in-patient care (BICUs, on ventilator, step down from BICU) across the U.S. **Aim 2**: was to assess the efficacy of a personalized, structured, and quantifiable exercise program (MP10) implemented typically 4 to 5 days after the first surgical operation after admit (or when burn surgeon deems mobilization to be safe), and during the entire BICU, on ventilator and in-hospital stay in burned individuals.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Exercise, burns, standard of care, MP10, early exercise, lean mass, muscle strength, 6-minute walk

3. ACCOMPLISHMENTS:

What were the major goals and objectives of the project?

Aim 1 was to characterize, via a survey(s) the Standard of Care of in-patient care (BICUs, on ventilator, step down from BICU) at the 4 sites (UTMB-Galveston, USAISR, UTSW-Dallas, UC Davis). Aim 1 was completed at 100 completion.

Aim 2 was to assess the efficacy of a personalized, structured, and quantifiable exercise program (MP10) implemented typically 4 to 5 days after the first surgical operation after admit (or when burn surgeons deems mobilization to be safe) and during the entire BICU, on ventilator and in-hospital stay in burn individuals. Aim 2 is ongoing, even after the end of the funded period. Specifically, data analyses continue to be conducted in preparation of a manuscript(s) or abstract(s). We estimate that it is at 85% completion. When the manuscript is submitted for publication it will be 95% completion. When manuscript is accepted for publication, it will be 100% completion.

What was accomplished under these goals?

Aim 1 was accomplished by sending surveys to each of the sites via each site’s PI. The PI then delegated the survey to the appropriate staff to fill out. It resulted in one publication. The details of the publication are as follows: Strength and Cardiorespiratory Exercise Rehabilitation for Severely Burned Patients During Intensive Care Units: A Survey of Practice. Cambiaso-Daniel J, Parry I, Rivas E, Kemp-Offenberg J, Sen S, Rizzo JA, Serghiou MA, Kowalske K, Wolf SE, Herndon DN, Suman OE. J Burn Care Res. 2018 Oct 23;39(6):897-901.

We designed a survey investigating exercise rehabilitation programs (RP) in the ICU for burn patients with $\geq 30\%$ total burned surface area. The survey was composed of 22 questions and submitted electronically via SurveyMonkey® to six major (pediatric and adult) burn centers in Texas and California. All centers responded and reported exercise as part of their RP on the ICU. The characteristics of exercises implemented were not uniform. All centers reported to perform resistive and aerobic exercises but only 83% reported isotonic and isometric exercises. Determination of intensity of exercise varied with 50% of centers using patient tolerance and 17% using vital signs. Frequency of isotonic, isometric, aerobic, and resistive exercise was reported as daily

by 80%, 80%, 83%, and 50% of centers, respectively. Duration for all types of exercises was extremely variable. Mobilization was used as a form of exercise by 100% of burn centers. Our results demonstrated that although early RP seem to be integral during burn survivor's ICU stay, no SOC exists. Moreover, early RP are inconsistently administered and large variations exist in frequency, intensity, duration, and type of exercise. Thus, we concluded that future prospective studies investigating the various components of exercise interventions were needed to establish a SOC and determine how and if early exercise benefits the burn survivor.

The list of questions on the survey were as follows:

Early Exercise and Ambulation Protocol Questions

1. What patient demographics do you provide services for at your burn center?
 - a. Children (0-17 years)
 - b. Adults (18 years and above)
 - c. Both children and adults

2. What is your annual burn admission at your burn center?
 - a. Children _____
 - b. Adults _____

3. What is the average percentage of TBSA for your burn admissions?

4. Are you an American Burn Association Verified Burn Center?
 - a. Yes
 - b. No

5. What is your intensive care unit inpatient to therapist ratio?

6. Please indicate on what day does the burn rehabilitation therapist (OT/PT) first mobilize the burn patient post burn injury admission? (Mobilize refers to movement of any extremity or the entire body).

7. What is the frequency of rehabilitation therapy session for the burn patient post burn injury admission while in the burn intensive care unit (BICU)?
 - a. Once a day
 - i. Yes
 - ii. No
 - b. Twice a day
 - i. Yes
 - ii. No
 - c. 2-3 times a week
 - i. Yes
 - ii. No
 - d. 5 times a week
 - i. Yes
 - ii. No
 - e. 7 times a week
 - i. Yes
 - ii. No

8. What types of exercises does the therapist initiate post burn injury admission while in the BICU? Check all that apply.
- a. Isotonic exercise (Active, passive, active assistive range of motion)
 - i. Yes
 - ii. No
 - b. Isometric exercise (Muscle contraction)
 - i. Yes
 - ii. No
 - c. Resistive exercise
 - i. Yes
 - ii. No
 - d. Aerobic exercise
 - i. Yes
 - ii. No
 - e. Other_____
9. When do you traditionally initiate ambulation post burn admission to the BICU?
(Please indicate by the number of day i.e. day 1, day 2, day 3 etc.)
10. When do you traditionally initiate ambulation post upper extremity grafting?
(Please indicate the number of day i.e. day 1, day 2, day 3 etc.)
11. When do you traditionally initiate ambulation post lower extremity grafting?
(Please indicate the number of day i.e. day 1, day 2, day 3 etc.)
12. Does the therapist include ace wrapping or elastic wrap bandaging to the lower extremities in preparation for getting a patient out of bed to ambulate in the BICU?
- a. Yes
 - b. No
13. Does the therapist include any therapeutic interventions in preparation for getting a patient out of bed to ambulate?
- a. Yes
 - b. No
14. If answered yes above, what therapeutic interventions are performed to prepare the burn patient for ambulation?
- a. Dangling edge of bed
 - b. Weight bearing activities
 - c. Tilt table
 - d. Standing frame
 - e. Other_____
15. Does rehabilitation at your burn center include ambulation of the ventilated burn patient?
- a. Always
 - b. Sometimes
 - c. Rarely
 - d. Never

16. What assistive devices are utilized to assist the burn patient in early ambulation if necessary? Check all that apply.
- a. Walker/front wheeled walker
 - i. Yes
 - ii. No
 - b. IV pole
 - i. Yes
 - ii. No
 - c. Crutches
 - i. Yes
 - ii. No
 - d. Cane
 - i. Yes
 - ii. No
 - e. Wheelchair
 - i. Yes
 - ii. No
 - f. Other_____

17. Do you ambulate burn patients with any of the following devices? Check all that apply.
- a. Unna's boots
 - i. Yes
 - ii. No
 - b. Splints
 - i. Yes
 - ii. No
 - c. Casts
 - i. Yes
 - ii. No
 - d. Knee immobilizers
 - i. Yes
 - ii. No
 - e. Other_____

18. For each type of exercise, what is the actual frequency of performing the following exercises with your burn patients with TBSA 30% or higher? (For example: Daily, Monday/Wednesday/Friday or Tuesday/Thursday)

19. For each type of exercise, how do you decide on the intensity of exercise to be performed for the following? (For example: a 6 minute walk, graded exercise treadmill test)

20. For each type of exercise, how do you measure the intensity while performing the following exercise with your burn patients? (For example: RPE's)

21. What is the duration of each type of exercise performed with your burn patients? (For example: 30 seconds on, 30 seconds off)

22. What machine or devices are utilized in performing the exercise indicated below? (For example: stretch bands, variable resistance machine or medicine ball weights i.e. 5 lbs)

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Conclusions were that future prospective studies investigating the various components of exercise interventions were needed to establish a SOC and determine how and if early exercise benefits the burn survivor.

Aim 2 was to assess the efficacy of a personalized, structured, and quantifiable exercise program (MP10) implemented typically 4 to 5 days after the first surgical operation after admit (or when burn surgeons deems mobilization to be safe) and during the entire BICU, on ventilator and in-hospital stay in burn individuals. Aim 2 is ongoing. Specifically, data analyses continue to be conducted in preparation of a manuscript(s) or abstract(s). We estimate that it is at 85% completion. When the manuscript is submitted for publication it will be 95% completion. When manuscript is accepted for publication, it will be 100% completion.

Inclusion study criteria was:

1) Age ≥ 7 to 60 years; and 2) Burns covering $\geq 30\%$ of the total body surface area (TBSA)

Information on enrollment numbers across sites (number of adults, pediatric, enrolled, completed, withdrew, died, SOC, SOC+MP10, etc.).

Study Site: UTMB/SHC-Galveston

Total number of participants = 54

Adults--- Number of adults participating = 3
Number adults enrolled = 4
Number of adults completing study = 3
Number of adults withdrawing = 1
Died= 0
Standard of Care (SOC) = 2
SOC + MP10 (Mobility Program) = 1

Children--- Number of children participating = 51
Number children enrolled = 57
Number of children completing study = 51
Number of children withdrawing = 5; an additional child did not withdraw. Shriners stopped research
Died= 2
Standard of Care (SOC) = 15
SOC + MP10 (Mobility Program) = 36

Study Site: UCD/SHC-NCA

Total number of participants = 13

Adults--- Number of adults participating = 0
Number adults enrolled = 0
Number of adults completing study = 0
Number of adults withdrawing = 0
Died= 0
Standard of Care (SOC) = 0
SOC + MP10 (Mobility Program) = 0

Children--- Number of children participating = 13
Number children enrolled = 14
Number of children completing study = 13
Number of children withdrawing = 1
Died= 0
Standard of Care (SOC) = 4
SOC + MP10 (Mobility Program) = 9

Study Site: UTSW/Parkland

Total number of participants = 5

Adults--- Number of adults participating = 5
Number adults enrolled = 9
Number of adults completing study = 5
Number of adults withdrawing = 4
Died= 0

Standard of Care (SOC) = 2
SOC + MP10 (Mobility Program) = 3

Children--- Number of children participating = 0
Number children enrolled = 0
Number of children completing study = 0
Number of children withdrawing = 0
Died= 0
Standard of Care (SOC) = 0
SOC + MP10 (Mobility Program) = 0

Study Site: USAISR

Total number of participants = 5

Adults--- Number of adults participating = 5
Number adults enrolled = 5
Number of adults completing study = 5
Number of adults withdrawing = 0
Died= 0
Standard of Care (SOC) = 2
SOC + MP10 (Mobility Program) = 3

Children--- Number of children participating = 0
Number children enrolled = 0
Number of children completing study = 0
Number of children withdrawing = 0
Died= 0
Standard of Care (SOC) = 0
SOC + MP10 (Mobility Program) = 0

**Grand total of subjects completing the study is 77. Of these 13 are adults and 64 are children.
25 SOC versus 52 SOC + MP10**

UTMB IRB and Shriners Headquarters in Tampa, FL implemented suspensions of all burn research activities as of 28 November 2018 for pediatric patients at Shriners and as of 4 December 2018 for pediatric and adult patients admitted to UTMB. This stoppage of enrollment by UTMB and by Shriners affected enrollment for the UTMB site, but also affected other sites as they did not want to proceed without the lead site's participation. Additionally, the DOD also stopped further enrollment until investigation and audit reports were completed. These stoppages significantly impacted our ability to recruit or enroll new patients.

An additional problem that was encountered was that we had no access to Shriner patients data or information other than the one in their paper exercise folders. Thus if data was missing from the folders, we had no way of accessing the data that could have been found inside the computers housing the equipment that gathered the data. For example the DEXA computer for body composition, the treadmill time for treadmill test, or the actual technicians/coordinator notes on the 6-minute walk. Not all of the data collected at Shriners site was accessible for analysis later since the Shriners site is now separate from UTMB. This data included DEXA results for four participants. Thus, the study was impacted by the suspension in terms of participant recruitment, other sites willingness to continue without our IRB approving of the project, and due to the DOD decision to stop enrollment until an independent biostatistician gave his/her opinion. If the biostatistician would have suggested

that enrollment could continue, perhaps we would have found significance in various outcomes. It is important to note that the PI completed all required steps to the best of his ability being that the Office of Institutional Compliance had all the details of the investigation in their control. Because of the greater number of admits to the ICU at Shriners compared to adults admitted to UTMB, the suspension of Shriners significantly affected enrollment numbers. Additionally, due to Shriners not allowing the PI access to data on computers housed at Shriners, some of the missing values are not retrievable.

In spite of this, we have prepared based on preliminary analyses three posters to be potentially submitted for consideration for the 2021 American Burn Association annual meeting. These three posters form the basis of our intended manuscripts.

Abstract ONE

This study aimed to evaluate the safety of aerobic exercise to improve functional outcomes (aerobic capacity and daily activity levels) of burn patients receiving an exercise program plus standard of care in the burn intensive care unit. We hypothesized that the burn intensive care unit exercise program plus standard of care group would not show a statistically significant decrease in functional outcomes compared to the standard of care group without exercise group. In other words, exercise in the ICU would be safe. This unblinded randomized, controlled study consisted of 56 patients with complete data. There were 35 patients in the standard of care (SOC) plus burn intensive care unit (BICU) exercise program and 13 patients in the SOC alone group. The study included patients from 7 to 22 years of age with $\geq 30\%$ total body surface area (TBSA) burns. Measurements were taken early after BICU admission and again at discharge (within 3 weeks after hospital discharge or within 1 week of scheduled discharge). Standard of care consisted of physical and occupational therapy. The BICU exercise program included sessions 5 days a week, 2 times a day for 10 minutes each. Lower extremities were trained in the morning and upper extremities were trained in the afternoon. Training sessions were based on the Borg rated perceived exertion (RPE) from 3 (Moderate) to 5 (Strong) intensity, reported when using the ergometer. Aerobic Capacity was measured via the treadmill test, which used the standardized, modified Bruce treadmill protocol. Measurements such as maximum oxygen uptake (VO_2 max) and oxygen uptake at rest (VO_2 rest) were recorded during the treadmill test. Daily functional mobility was measured via the portable activity monitors called pedometers (Fitbit Zip). Measurements such as total steps taken and total miles traveled were recorded by the pedometers. Analysis used paired t-tests and Wilcoxon signed-rank tests. Significance was set at $p < 0.05$. All data reported as mean \pm standard deviation. Both Age (EX + SOC 12.2 ± 3.5 years, SOC 12.2 ± 3.2 years, $p = 0.113$) and total body surface area burned (EX + SOC $48 \pm 14\%$, SOC $53 \pm 18\%$, $p = 0.210$) were comparable between the two groups. There was no statistically significant difference between both groups for average VO_2 Rest or average VO_2 Max. There was no statistically significant difference between both groups for total steps taken or total miles traveled. The BICU exercise group did not significantly differ from the SOC group in any measures. Thus, though ergometric aerobic exercise was safe and did not cause decreases in the functional outcomes achieved in the BICU exercise group, this exercise program was not effective in causing increases in functional outcomes compared to SOC alone. Though further data collection is required before making a definite conclusion, future research should investigate aerobic exercise in the BICU plus resistance exercises and/or anabolic agents (e.g. oxandrolone) as a means of improving functional outcomes.

Authors and their affiliations were as follows:

Alec Hasty^{1,2}, Christian Tapking^{1,3}, Shauna Q. Glover^{1,3}, Danny Tran^{1,2}, Chris Luzania^{1,3}, Angela Angudelo^{1,3}, Amy Givan⁴, David Herndon^{1,3}, Oscar E. Suman^{1,3}

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Abstract TWO

In this single center UTMB study, we compared the clinical outcomes (length of stay, length of ventilation, lean body mass, and psychosocial health) of patients who received ergometric exercise in addition to standard of care (EX) to patients who received the standard of care only (SOC). We hypothesized that the EX group will have statistically significantly improved clinical outcomes at discharge compared to the SOC group. 56 patients between ages 7 and 22 with $\geq 30\%$ total body surface area (TBSA) burned were randomized to a 2:1 ratio of EX (n=35) to SOC (n=13). The SOC group received physical and occupational therapy as part of the standard of care. The EX group performed ergometric exercises on a ergometer twice a day for 5 days a week in addition to receiving the SOC. The intensity of the workout was maintained between 3 and 5 on the Borg Rating of Perceived Exertion scale. Lean body mass was evaluated via dual energy x-ray absorptiometry (DEXA) at admission and discharge. Psychosocial health was evaluated by the Pediatric Global Health 7 from PROMIS before (Pre) and after (Post) the initial set up (Acute) and last work out session (DC). Age (EX 12.2 ± 3.47 years, SOC 12.2 ± 3.17 years, $p=0.1134$) and total body surface area burned (EX $48 \pm 14\%$, SOC $53 \pm 18\%$, $p=0.2104$) were comparable between the two groups. Length of stay (EX 39.89 ± 24.07 days, SOC 43.12 ± 20.57 days, $p=0.7327$), length of ventilation (EX 4.1 ± 5.2 days, SOC 7.4 ± 9.4 days, $p=0.0962$), lean body mass (EX 35.09 ± 12.91 Kg, SOC 27.63 ± 10.59 Kg, $p=0.0885$) and psychosocial health (EX DC Post 0.95 ± 0.165 , SOC DC Post 0.94 ± 0.113 , $p=0.9514$) were not significantly different between groups. Psychosocial health did show improvement over time when comparing acute vs discharge for both pre (EX Acute 2.66 ± 0.084 vs. EX discharge 1.40 ± 0.167 , $p \leq 0.0001$, SOC acute 3.10 ± 0.235 vs. SOC discharge 1.72 ± 0.344 , $p \leq 0.0001$) and post exercise (EX Acute 2.14 ± 0.189 vs. EX discharge 0.95 ± 0.165 , $p \leq 0.0001$, SOC acute 2.00 ± 0.148 vs. SOC discharge 0.94 ± 0.113 , $p=0.0051$). At this point, ergometric exercises did not appear to have a significant impact on patient length of stay, lean body mass, and psychosocial health. These findings suggested that ergometric exercise was not more effective than the SOC alone on improving clinical outcomes in the BICU setting at the moment. However, the study analyses was still ongoing and was missing the Sacramento and the data on the adult population from other institutions. Presently, our conclusions seem to remain the same. No adverse events were noted at any of the sites.

Authors and their affiliations were as follows:

Danny Tran^{1,2}, Christian Tapking^{1,3}, Chris Luzania^{1,3}, Angela Angudelo^{1,3}, Alec Hasty^{1,2}, Shauna Glover^{1,3}, David Herndon^{1,3}, Oscar E. Suman^{1,3}

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Abstract THREE

The purpose of this evaluation was to compare the 6-minute walk test versus the Bruce modified protocol. The American Cardiothoracic Society has stated that the six-minute walk test is a good substitute for more intense cardiopulmonary exercise in patients with pulmonary pathologies. Distance walked has been shown to be a good indicator of maximal oxygen consumption (VO₂ max) in these patients. We assessed whether the six-minute walk test would show similar results in pediatric burns. Methods: Twenty-five patients 7-18 years of age enrolled in the multi-center MP-10 trial who had a 6-minute walk test and a modified Bruce protocol treadmill test were included. Six-minute walk outcomes included: heart rate post walk, and distance walked, these were compared with Spearman's rank-order correlations to treadmill test outcomes: VO₂ max, work, distance, and heart rate at VO₂ max. Co-variates included age, total burn surface area, inhalation injury, and body mass index. Results: All patients had good effort on the treadmill as judged by heart rate reserve. While heart rate post walk did correlate with heart rate at VO₂ max (Spearman coefficient: 0.69, $p < 0.01$), walk distance had poor correlation with VO₂ max (Spearman coefficient = -0.16, $p = 0.47$). VO₂ predicted by the 6 minute walk had poor correlation with actual VO₂ (Spearman coefficient = -0.11, $p = 0.64$). Distance walked had poor correlation with treadmill distance (Spearman coefficient = 0.16, $p = 0.46$) and treadmill work (Spearman

coefficient = 0.05, $p = 0.81$). Conclusions: In our study, the six-minute walk had poor correlation with indirect calorimetry. Although heart rates did correlate, no correlation was demonstrated in outcomes of VO₂, distance, and work. Though initially promising, the six-minute walk may be a poor early predictor of exercise capacity in pediatric burn patients. If available, cardiorespiratory capacity should be assessed using standard treadmill tests with indirect calorimetry following the Bruce protocol. However, if the patient cannot perform a treadmill test, then the 6-minute walk test is appropriate.

Authors and their affiliations were as follows:

Christian Sommerhalder, Shauna Glover, Angela Agudelo, Stuart. S Jackson, Christian Tapking, David N. Herndon, Oscar E. Suman

All authors were from UTMB and Shriners Hospital for Children in Galveston.

These abstracts were all prepared in October 2018 for submission to the ABA. They were part of the preliminary analyses efforts. However, UTMB/Shriners mandated their withdrawal from consideration to present at the ABA, thus for the 2019 ABA these were not presented. Presently, we are planning on submitting our latest findings which are from all 4 sites and includes their data.

What opportunities for training and professional development has the project provided?

The project has offered the opportunity for medical students and post-doctoral research fellows to learn about research, exercise testing and training, statistics, manuscript/abstract submission, and presentation.

How were the results disseminated to communities of interest?

The results were disseminated to communities of interest via oral presentations at the ABA and ISBI. Also the results were disseminated via peer-review publication with another 1-3 publications planned in the very near future.

What do you plan to do during the next reporting period to accomplish the goals?

Nothing to report.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

A potential change in practice will hopefully result from this study. Shriners Hospital for Children in Galveston is presently restructuring its clinical research program. As of now, we do not know if results from this project will result in any changes in standard practice. We hope to disseminate our findings at the American Burn Association and/or the International Society for Burn Injuries Annual Meeting in 2021. At those meetings we hope to suggest to the audience that exercise in the ICU is safe, though more research is needed to find the optimal and effective type, amount and intensity of exercise. At UTMB, exercise training and testing is being highly considered, but is undergoing logistical analysis (space, personnel, funds, etc).

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report.

What was the impact on society beyond science and technology?

Nothing to Report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Issues that affected enrollment were stoppage of enrollment by UTMB and by Shriners. Enrollment was first stopped due to 3 whistleblowers complaints about potential unethical practices unrelated to this project. This was as explained in the newspaper. This stoppage was on November 28, 2018 at Shriners Hospital and on December 4, 2018 at UTMB. Actions taken to overcome the stoppage was to collaborate fully with the Office of Institutional Compliance at UTMB. This study underwent a full external and independent review/audit by Ankura. No major issues were found with this study and it was cleared to go forward. This occurred in July 2019. However, before proceeding, there were numerous steps to follow.

The suspensions impacted/changed the research by limiting our enrollment and access to data if data was missing in paper records, but available on computer servers or drives. Enrollment was on hold for 13 months (one month in December 2018 and all of 2019). Enrollment was closed and remained closed for all of 2019. When the DOD and UTMB agreed to go forward in late 2019 (December) it was to analyzed data from all sites. This was done without re-opening enrollment.

This completes the section “Actual or anticipated problems or delays and actions or plans to resolve them”.

Actual or anticipated problems or delays and actions or plans to resolve them

None.

Changes that had a significant impact on expenditures

Lack of enrollment at UTSW/Parkland and at USAISR prevented appropriate expenditure of funds. Funds from UTSW/Parkland were applied to UTMB and UC-Davis. The suspension from 12/6/18-July 2019 necessitated reversal of expenses that had previously posted to the project. Suspension of enrollment for this project which occurred in November 2018 also heavily impacted expenditures. That was the last time we enrolled participants.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

None.

Significant changes in use or care of human subjects

None.

Significant changes in use or care of vertebrate animals.

Not applicable

Significant changes in use of biohazards and/or select agents

Nothing to report

6. PRODUCTS:

Publications, conference papers, and presentations

We had three abstracts accepted for presentation at the 2019 ABA. All were withdrawn at the mandate of UTMB and Shriners.

We plan on submitting 1-3 abstracts to the 2021 ABA. One on safety, another on the physiological and psychosocial outcomes of MP10. The third one on 6-minute walk versus indirect calorimetry in MP10 patients.

Journal publications.

Cambiaso-Daniel J, Parry I, Rivas E, Kemp-Offenberg J, Sen S, Rizzo JA, Serghiou MA, Kowalske K, Wolf SE, Herndon DN, Suman OE. Strength and cardiorespiratory exercise rehabilitation for severely burned patients during intensive care units: A Survey of Practice. J Burn Care Res. 2018 [Mar 22, Epub ahead of print]. (PMC6151163)

Books or other non-periodical, one-time publications.

None

Other publications, conference papers, and presentations.

Submitted to the 2019 American Burn Association 51st International Conference in Las Vegas, and obtained acceptance of two abstracts pertaining to this study (AIM 2). The titles were:

1. *Safety of an Aerobic Exercise Program in the Burn Intensive Care Unit.
2. *Effects of Rehabilitation in Severely Burned Children in the Burn Intensive Care Unit

Both were withdrawn per order of compliance office and Provost. Both abstracts were based only on single center data, not the other 3 sites, and involved only pediatric patients.

Website(s) or other Internet site(s)

Nothing to report

Technologies or techniques

Nothing to report.

Inventions, patent applications, and/or licenses

Nothing to report.

Other Products

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Sourcing in the final year of the project.

For UTMB:

Name: Oscar Suman
Project Role: Project Director
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: 1.0 cal months (10%)
Contribution to Project: Dr. Suman continues to perform work in the area of maintaining regulatory compliance, monitoring exercise testing, and preparation of SOC survey.

Name: Michael Serghiou
Project Role: Consultant
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: not applicable
Contribution to Project: Mr. Serghiou has provided guidance to Dr. Suman in the preparation of the Survey of SOC.

Name: Ronald Mlcak
Project Role: Consultant
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: not applicable
Contribution to Project: Dr. Mlcak has provided guidance to Dr. Suman in the preparation of the protocol to the IRB on exercise in the ICU.

Name: Angela Agudelo
Project Role: Exercise Trainer
Researcher Identifier (e.g. ORCID ID): not applicable
Nearest person month worked: 1.0 cal months (100% for one month)
Contribution to Project: Angela Agudelo has provided the exercise training sessions and visiting sessions to all patients in the MP10 project, as well as assisted in assessments.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Yes.

What other organizations were involved as partners?

Organization: University of California – Davis
Location: 1850 Research Park Dr. Ste. 300, Davis, CA 95618-6153

Contribution to the Project: Collaboration

Organization: The University of Texas Southwestern Medical Center at Dallas

Location: 5323 Harry Hines Blvd., Dallas, TX 75390-9105

Contribution to the Project: Collaboration

Organization: US Army Institute of Surgical Research

Location: 3698 Chambers Pass, Ft. Sam Houston, TX 78234-6315

Contribution to the Project: Collaboration

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.

- 9. APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Other Support

Suman, Oscar E

Current

W81XWH-14-2-0162 Suman (PI) 09/30/14-12/31/20 0.24 cal mths
Dept of Defense \$189,027

"Identification and Validation of Established and Novel Biomarkers for Infections in Burns"

Goal: To improve clinical care for the severely burned Wounded Warriors and other burn victims.

Aims: 1) To determine plasma proteomic biomarkers for the prediction and diagnosis of sepsis using mass spectrometry techniques; use stable isotope techniques to detect proteins for which assays do not exist; 2) To validate already identified markers of infection in a multicenter study; 3) To develop a model of prediction of infection using clinical data and proteomic information.

Role: Principal Investigator

Contact: Eva Lai, PhD, Science Officer, eva.lai.ctr@mail.mil

Overlap: None

90DPBU0003-04-00 Wolf (PI) 09/30/17-09/29/22 0.60 cal mths
Natl Inst on Disability, Independent Living, and Rehab Res \$297,619

"Effects of anabolic steroids and blockade of chronic catecholamine mediated stress on psychosocial, growth, scar, and physiologic outcomes after massive burn injury"

Goal: Our long-term outcomes multicenter study fills a gap and provides knowledge about the prevalence of emotional and physical disabilities among pediatric or adult survivors of burns suffered during childhood and evaluating the impact of advancements in burn care and rehabilitation on survivors' quality of life and reintegration.

Aims: Data collection for Specific Aim 1: NIDILRR Questionnaire which includes demographic data, VR-12(Veterans RAND), PHQ(Patient Health), CIQ(Community Integration), SL(Satisfaction with life Scale),5-D Itch Scale, etc. Specific Aim 2: Blood samples or buccal swabs. Genomic DNA will be isolated using a DNA extraction kit. The adrenergic and androgen receptors will be evaluated for clinically and functionally relevant SNP's. Specific Aim 3: Physical Activity Monitors will assess the daily activity levels of patients. Specific Aim 4: Fasting plasma glucose and fasting plasma insulin.

Role: Co-Principal Investigator

Contact: Federal Project Officer: Dr. Kenneth Wood, 330 C Street SW, 2511B, Washington, DC 20201, (202) 275-7469; GMS: Patricia Barrett 202-795-7303, patricia.barrett@acl.hss.gov or Marlene Spencer 202-795-7422, marlene.spencer@acl.hhs.gov.

Overlap: None

W81XWH-15-1-0143 Branski (PI) 07/01/15-06/30/21 0.60 cal mths
Dept of Defense \$398,077

"Growth Hormone Therapy for Muscle Regeneration in Severely Burned Patients"

Goal: To determine whether restoration of depleted GH levels post-burn will lead to prevention of lean body mass loss and bone mineral content, improve rehabilitation, and accelerate reintegration of severely burned patients.

Aims: To determine the effects of recombinant human growth hormone (rhGH) supplementation on body composition, such as lean body mass loss and bone mineral content, and to assess if rehabilitation and subsequent reintegration of severely burned patients into society can be accelerated.

Role: Co-Investigator

Contact: Primary contact: Dr. Nicole Enman, Science Officer, CDMRP, Phone: (301) 619-7040, Email: nicole.m.enman.ctr@mail.mil

Overlap: None

Inactive

2R01 HD049471 (Suman)

02/01/15-01/31/20

2.28 cal mths

National Institutes of Health

\$64,560

"Oxandrolone and Exercise: A Potent Therapy in the Rehabilitation from Burns"

Goal: To identify evidence-based therapeutic interventions that are clinically effective in the rehabilitation and recovery of severely burned children.

Aims: 1) To determine the physiological therapeutic efficacy of exercise training/rehabilitation plus oxandrolone relative to exercise alone; 2) To determine the biochemical consequences of combined exercise training/rehabilitation and oxandrolone relative to those of exercise alone.

Role: Principal Investigator

Contact: Robert F. Tamburro, 6710B Rockledge Dr, Bethesda, MD 20817, 301-480-2619, robert.tamburro@nih.gov

Overlap: None

Early Mobility/Exercise Program (MP10) in the Burn Intensive Care Unit (ICU) Decreases Hospital Stay and Fatigue, and Improves Mental Health and Physical Performance

Proposal # 13214039 | Award # W81XWH-14-2-0160



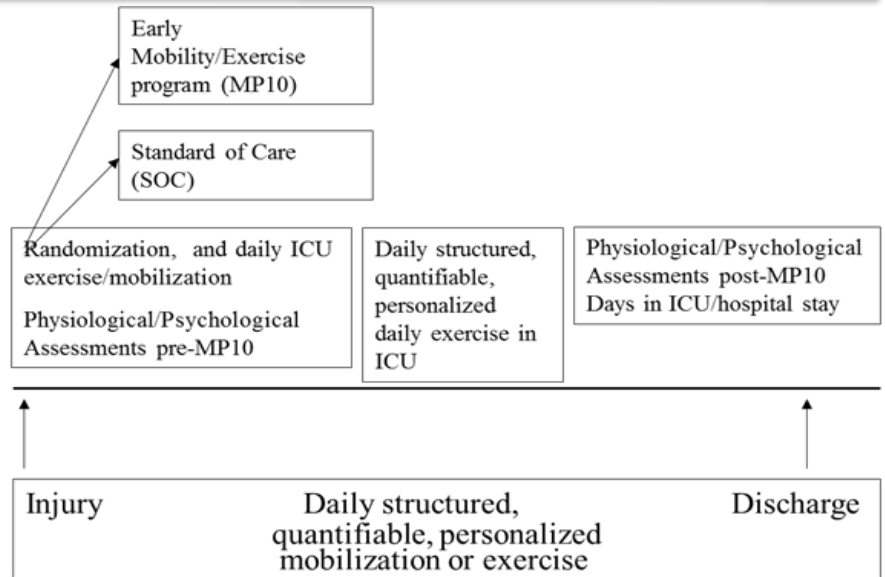
PI: Oscar E. Suman Org: The University of Texas Medical Branch/Shriners Hospital-Galveston Award Amount: \$1,079,350

Study/Product Aim(s)

- **Objectives:** 1) Decrease length of hospital stay. 2) Improve physiological and psychological outcomes.
- **Aim 1:** Characterize SOC in the ICU in each of the 4 sites. **Aim 2:** Test the hypothesis that early exercise in the ICU will significantly improve outcomes compared to SOC.
- **Outcomes:** Decreased ICU/hospital stay, improved lean mass, aerobic capacity/muscle endurance and fatigue scores.

Approach

Over 4 years, we will enroll 96 patients (24 per site; MP10 n=64 and SOC n=32) aged 18–60 years with ≥30% TBSA burns. Patients in MP10 will participate in a 10-minute leg-crank and a 10-minute arm crank ergometry session. Endpoints are lean body mass, cardiopulmonary and muscle endurance, length of BICU, ventilator and hospital stay, and Quality of Life.



Timeline and Cost

Activities	CY	1	2	3	4
a. Construction and development of Survey to characterize SOC; b. submit for peer-reviewed publication					
Implement MP10+SOC vs SOC, obtain IRB, HRPO, register for clintrials.gov, enroll patients					
Submit manuscripts, present posters or oral presentations					
Estimated Budget (\$K)		296K	255K	262K	267K

Goals/Milestones

- CY1 Goal** – IRB and HRPO approval for UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA
Survey completion to characterize SOC completed by UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA
- CY2 Goals** – MP10 enrolling at UTMB/SHC-GAL; UTSW; and UCD/SHC-NCA
Submission of abstract on Survey to ISBI
- CY3 Goal** – Continuation of MP10; Submission of manuscript (Aim 1)
- CY4 Goal** – Continuation of MP10
Analysis of data, submission of abstracts to ABA, ISBI or other critical care meetings. Submission of manuscript(s). (Aim 2)

Comments/Challenges/Issues/Concerns

- Study re-open to data analysis only.

Budget Expenditure to Date

Actual expenditures: 825,619.78
Projected expenditures: 1,079,349.00