Exertional Rhabdomyolysis:
Effect of High Intensity Exercise

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Introduction:

A global rise in healthy trends has led more individuals to engage in exercise regimens to improve their overall fitness. Exercise is a tool with known benefits of building cardiovascular endurance, bone integrity, and weight maintenance. With proper design, an exercise program can promote a healthy lifestyle that is beneficial to whomever is engaging. Unknown to many, however, an improper exercise program can be detrimental to one's health. Exertional rhabdomyolysis is a multifactorial medical condition that results secondary to an exercise regimen.

Pathophysiology

Exertional rhabdomyolysis is the breakdown of skeletal muscle secondary to exercise. In the setting of exertional rhabdomyolysis, major muscle groups break down and leak electrolytes, myoglobin, and other proteins into the bloodstream. These muscle contents in the bloodstream can be measured as serum creatine kinase (CK).[1] As the muscle contents are leaked into the bloodstream, serum CK levels rise. Exertional rhabdomyolysis is diagnostically defined as an inappropriate elevation in serum CK as a direct result of physical exertion.

Clinical Presentation and Physical Exam

The clinical presentation of exertional rhabdomyolysis varies which can be a challenge for clinicians. The classic triad includes myalgias, generalized weakness and tea-colored urine due to myoglobinuria. Symptoms may also include fatigue, nausea, vomiting and fever. Severe manifestation may include delirium and oliguria. [2] Clinical presentation can occur anywhere from 12 to 48 hours after exercise is completed. With history and clinical presentation, clinicians should have a suspicion for the possibility of exertional rhabdomyolysis.

The physical exam of exertional rhabdomyolysis is often nonspecific. Possible physical exam findings may include decreased muscle strength, and soft tissue swelling and bruising.

Compartment syndrome may concurrently present early or late in exertional rhabdomyolysis. A tender, firm muscle compartment with focal neurologic findings and diminished distal pulses should quickly raise suspicion for compartment syndrome.[2]

Diagnosis

Diagnosing exertional rhabdomyolysis begins with clinical suspicion, but also includes testing for a serum diagnostic marker with serum CK. Serum creatine kinase elevates and peaks at 24 to 36 hours after exertion. The serum creatine kinase levels then return to baseline at an estimated rate of around 40% per day.[2] The elevation of creatine kinase is common after exercise and does not always lead to exertional rhabdomyolysis. In a non-exercising individual, the normal range of serum creatine kinase is 10 to 205 IU/L. After intense exercise, creatine kinase levels can elevate as high as 20,000 IU/L. There is some debate on the level of serum creatine kinase to diagnose exertional rhabdomyolysis. However, it is generally accepted that a level of serum creatine kinase above 5,000 IU/L should warrant the diagnosis of exertional rhabdomyolysis. [2]

In the suspicion of exertional rhabdomyolysis, additional diagnostic tests should be performed. Additional diagnostic tests include serum potassium, blood urea nitrogen (BUN), creatinine, urine myoglobin, and electrocardiogram (ECG). Hyperkalemia can indicate muscular damage and increases the risk for cardiac dysrhythmias. Elevated serum BUN and creatinine are indicators of renal function and hydration status. Urine myoglobin indicates muscular damage, but the absence of urine myoglobin does not exclude exertional rhabdomyolysis. An ECG assesses for cardiac dysrhythmias that can occur with electrolyte abnormalities; the most common ECG findings are associated with hyperkalemia which includes peaked T waves, wide and flat P waves, and prolonged PR intervals. [2]

Associated Complications

Exertional rhabdomyolysis can result in complications that may be severe. One severe complication of exertional rhabdomyolysis is electrolyte abnormalities including hyperkalemia, hypocalcemia, hyperphosphatemia, and hyperuricemia. [2] The electrolyte imbalances are the leading cause of dysrhythmias that occur in this setting. Compartment syndrome is also a serious complication associated with exertional rhabdomyolysis. Increased edema within the muscle compartment results in a rise of compartment pressure. A compartment pressure greater than 50 mm Hg or pressure between 30- and 50-mm Hg for longer than six hours will require a surgical consultation. A decompressive fasciotomy will be considered in patients with compartment syndrome to decrease likelihood of muscle necrosis. Another alarming complication of the condition is acute kidney injury. Acute kidney injury (AKI) is the result of myoglobin causing renal vasoconstriction, nephrotoxic effects and renal tubular obstructions. Prolonged AKI will lead to acute tubular necrosis with potential of irreversible damage to the kidneys. Metabolic acidosis is another complication that may also occur in the setting of exertional rhabdomyolysis. [3] Individuals who have little or no urine output despite hydration, profound acidosis, or severe hyperkalemia will be candidates for peritoneal dialysis or hemodialysis. [2]

Exertional rhabdomyolysis is one category of rhabdomyolysis where there has been muscle injury as a direct cause from exercise. According to Eichner, "When it comes to exertional rhabdomyolysis, however, only one common cause exists: too much, too fast, too soon of an exercise too novel."[2] In most cases exertional rhabdomyolysis is a multifactorial condition. Risk factors include inadequate hydration, recent inactivity, high ambient temperature, and use of supplements. The risk of exertional rhabdomyolysis increases with heat illness due to the propensity for dehydration, but the condition can occur at any temperature. As more factors contribute to the condition, an increase likelihood of exertional rhabdomyolysis will occur.

Epidemiology

As the popularity of intense exercise increases, the risk of injury or illness associated with exercise also increases. The concern for exertional rhabdomyolysis should be associated with individuals who engage in rigorous physical activity. The prevalence of rhabdomyolysis in the United States is reported as 26,000 cases with 47% falling under the diagnostic criteria of ERM.[4] Exertional rhabdomyolysis can be seen in any setting of exercise although most cases are related with endurance events and high-repetition weight training.[2] The Armed Forces is one patient population where cases of exertional rhabdomyolysis have been reported. The subgroup where incidence rates are the highest are with service members in the Marine Corps and Army. [5] Service members are at a high risk for developing the condition due to the vigorous physical demand endured.

Another setting in which exertional rhabdomyolysis cases are reported is within athletics, collegiate athletics, in particular. The athletic demand placed on athletes by athletic coaches or strength coaches along with design of conditioning programs predispose athletes to exertional rhabdomyolysis. Two additional areas where incidence is increasing is with CrossFit and spinning programs. Individuals who engage in these programs under the design of a coach are following patterns of a high intensity interval training (HIIT) regimen which increases the likelihood of developing exertional rhabdomyolysis.

Risk Factors

Various risk factors contribute to the development of exertional rhabdomyolysis. One factor associated with the condition is the type of physical activity in which the individual is engaged. A common trend is training regimens that focus on total muscular fatigue and eccentric contractions.[2] Eccentric contractions occur when a muscle actively lengthens such as downhill running or lowering of a weight.[6] More human research is needed to further explore the association of exertional rhabdomyolysis with specific training methods. Another risk factor is the conditioning status of the individual. A common history with exertional rhabdomyolysis is heavy and unaccustomed exercise. Even though unaccustomed exercise is a risk factor for developing exertional rhabdomyolysis, the condition can occur in trained athletes. The use of dietary supplements, mainly ephedra, creatine, and herbal weight loss supplements, also increase the individual's risk for development of the condition. Dietary supplements have a tendency to lead to dehydration which is a known trigger of rhabdomyolysis.[2] Genetics may also play a role in exertional rhabdomyolysis. The genetic link has been associated with polymorphisms of creatine kinase muscle isoform, alpha-actinin 3, and myosin light kinase 2. [2]

Clinical Question

The growing popularity of engaging in exercise is overall an asset in promoting healthy lifestyle behaviors. However, exercise can have negative impact including the risk of exertional rhabdomyolysis. Exertional rhabdomyolysis was once a condition associated with the physical demand of military services. Given the trend of high intensity exercise programs, the prevalence of exertional rhabdomyolysis is increasing. The purpose of this paper is to look at the prevalence of exertional rhabdomyolysis with relevance to a particular exercise program. We aim to answer the question: Does a high intensity eccentric exercise program increase the risk of developing exertional rhabdomyolysis?

Methods:

Primary literature for the topic exertional rhabdomyolysis is scarce which limits the quality of this research. The vast majority of research on exertional rhabdomyolysis is limited to case reports. Research on exertional rhabdomyolysis was conducted through search engines including PubMed, Embase and Cochrane Library. The MeSH terms used were "exertional rhabdomyolysis", "exercise induced rhabdomyolysis", "effect of exercise on exertional rhabdomyolysis", and "exertional rhabdomyolysis high intensity exercise". The reference list of articles chosen for this research were also analyzed for any possible relevant articles to also be included. The Cochrane Risk of Bias Tool was used to evaluate the primary literature.

Results:

The search strategy yielded one experimental trial and five case reports which were utilized in this research. The primary literature focuses on the severity of exertional rhabdomyolysis and the effect on muscle performance. The case reports analyze series of exertional rhabdomyolysis incidences to determine the cause and effect of the condition. The primary literature and case reports are discussed with high yield information summarized in Tables 2, 3, and 5.

Primary Literature

Hody et al. 2013[7]

Hody et al. performed an experimental trial to examine the severity of exertional rhabdomyolysis and its correlation with muscle performance in the setting of maximal eccentric exercise. The trial further examined how the relationship between eccentric exercise, muscle fatigue and exertional rhabdomyolysis can predict a CK response before clinical symptoms are present. Table 1 describes characteristics of the experimental trial.

Table 1 Characteristics of Primary Literature

Methods	
Participants	27 volunteers: sedentary/moderately active, healthy men **Trial parameters:** no vigorous/unusual physical activity or medication usage **Inclusion criteria:** no history of LE[a] injury or participating in exercise program **Exclusion criteria**: none listed **Setting:** University Hospital Centre of Liége **Duration:** Not provided
Interventions	**Warm up protocol:** 10 minutes - bicycle ergometer, 3 sets of 5 submaximal quadricep concentration contraction at 120˚/s throughout constant ROM[a], 3 sets of 5 quadricep eccentric contractions at 60˚/s **Exercise Protocol:** 3 sets of 30 maximal quadricep eccentric contraction at 60˚/s throughout same ROM[a]; 30 second rest in between sets
Outcomes	Muscle fatigue, muscle damage, CK[a] activity, DOMS[a], muscle stiffness
Notes	**Statistical Analysis** – plasma CK[a] activity: 10 (log), pre and post CK differences: paired Student's *t*-test; Pearson's correlation coefficient: relationships between parameters; differences between HR[a], MR[a], LR[a] groups: ANOVA; individual comparison: Tukey's post-hoc test; statistical significance = P<0.05 **ITT analysis** – no details **Funding** – Fonds National de la Recherche Scientifique (FNRS) & Fonds Spéciaux de l'Université de Liége **Conflicts of interest** – S. Hody: FNRS Research Fellow; P. Leprince: FNRS Research Associate

Footnotes:
[a] *LE* – lower extremity, *ROM* – range of motion, *CK* – creatine kinase, *DOMS* – delayed-onset muscle soreness, *HR* – high respondent, *MR* – medium respondent, *LR* – low respondent

Hody et al. found a distinct relationship between eccentric protocols and elevation of plasma CK levels. The baseline mean log value of CK prior to the eccentric contraction repetition was 2.06 ± 0.24 IU/L. After one day of eccentric exercise, the CK activity increased significantly to 3.37 ± 0.77 IU/L (P <0.0001). To further analyze the results, subjects were placed into three groups based on their log CK response (high versus medium versus low responders) with statistically significant differences in CK activity in the pre- and post-measurements (Table 2).

Table 2 Summary of Results of Hody et al. 2013

	HR[b] (n=10)	MR[b] (n=8)	LR[b] (n=9)
log CK_{pre} (IU/L)	2.07 ± 0.29 [NS]	2 ± 0.19 [NS]	2.1 ± 0.25 [NS]
log CK_{post} (IU/L)	4.23 ± 0.25 ***	3.24 ± 0.14 ***	2.52 ± 0.27 ***
log CK_{post}/CK_{pre}	2.16 ± 0.4 ***	1.24 ± 0.11***	0.42 ± 0.25 ***

Footnotes:
[b] *HR* – high respondent, *MR* – medium respondent, *LR* – low respondent, *NS* – no significant difference between groups, *** - significant differences between groups

A correlation analysis was also performed between muscle fatigue parameters and plasma creatine kinase markers to better understand the relationship between log CK and muscle performance that showed a significant difference in fatigue, stiffness and work decrease (Table 3). The study not only determined CK response to eccentric exercise, but also the direct effect on muscle performance specifically during an unaccustomed eccentric workout.

Table 3 Results of Hody et al. 2013

	Log (CK_{post}/CK_{pre})	Stiffness (cm[c])	Soreness (a.u.[c])
Work set 1 (J[c])	0.320	0.386*	0.152
Work set 2 (J[c])	-0.209	-0.152	0.005
Work set 3 (J[c])	-0.583***	-0.474*	-0.215
Fatigue index 1	0.816***	0.754***	0.329
Work decrease S1-S3[c]	0.835***	0.749***	0.372

Footnotes:
[c] *, *** indicate significant correlations (P<0.05, P<0.001), *a.u.* – arbitrary units, *cm* – centimeters, *J* – joules, *S1-S3* – set 1-set 3

The Cochrane Risk of Bias tool was utilized to evaluate the research quality of the trial. The results of the evaluation (Table 4) demonstrate the limitations of the study, including a small sample size and lack of randomization of subjects.

Table 4 Risk of Bias Analysis of Hody et al. 2013

Bias	Risk	Support for judgement
Random sequence generation	High risk	No randomization; no comparison group
Allocation concealment	Intermediate risk	Subjects volunteered, no comparison groups; random allocation did not occur
Performance bias	Low risk	No comparison group therefore blinding not pertinent
Detection bias	Low risk	Subjects separated into 3 groups based on log CK response: HR – log CK >1.54, MR – log CK between 0.93 and 1.54, LR – log CK <0.93
Attrition bias	Low risk	No withdrawals from study
Reporting bias	Low risk	All results were reported regardless of outcome

Summary of Case Reports

The case reports of exertional rhabdomyolysis included in this research demonstrate similarities suggestive that it is the type of exercise performed that is the key causative agent. In each of the case reports analyzed, the type of exercise performed followed an eccentric protocol (Table 5). The exercise regimens included either an upper extremity, lower extremity or complete body workout that focused on negative work which is known as eccentric contractions. The eccentric exercises were also completed at a timed maximum effort. Oh, et al. determined that the exercise regimen that 43 high school football players conducted in total was designed to be completed within 144 seconds without transition time between exercises. The average time the workout was completed with transition time and repeated intervals was four to five minutes.

The program did not include a recovery period in between exercises. In perspective, these high school football players performed eccentric exercises to fatigue for a continuous four-minute session.

With each case report, the individuals engaged in the activity were unaccustomed to the exercise being conducted. In both case reports of Smooth et al. and Stanfa et al., collegiate athletes were partaking in off season training that followed a break where organized workouts were minimal. The rest period was one to two weeks off from any required strength and conditioning workouts. Smooth et al. examined that the intensive offseason training program followed a 20-day break from any strength and conditioning workouts. On the first day of an intense three-day program, football players were required to perform timed 100 back squats at 50% of their one repetition maximum. Thirteen football players were hospitalized after this workout and subsequently more football players presented with clinical symptoms over the course of three days. Stanfa et al. similarly determined that an intense arm competition following a week off from training and a light week of their off-season strength program led female swimmers to experience exertional rhabdomyolysis. The arm competition included maximum pull-ups, rows, bench presses and pushups.

Despite these case reports only including subjects that were classified as athletic, the timing of the programs followed a rest period during which those performing the exercise may not have been acclimated to the demands of the program. Tibana et al. and Smooth et al. contributed case reports where sets of eccentric workouts were conducted within a close period, either within the same day or next day with limited recovery time in between workouts. The workouts were performed to fatigue and included similar muscle groups.

Table 5 Summary of Case Reports

Primary Author and Published Year	Subjects	Exercise Performed
Oh, 2012 [7]	43 high school football players; 6 hospitalized, voluntary CK[d] testing offered	Alternating chair-dip & push-up each for 30 sec, 20 sec, 10 sec, 7 sec & 5 sec; no rest sets; for incorrect performance exercise suspended and restarted
Oh, 2015 [8]	30 Army personnel admitted to Tripler Army Medical Center from Jan 2010-Dec 2012	12 cases: military training of physical fitness and ruck march 7 cases: physical training 5 cases: ruck march 4 cases: CrossFit 1 case: P90x
Smooth, 2013 [9]	78 collegiate football players at University of Iowa; 13 hospitalized; 10 players provided lab results	Sled pushes, weight lifting tasks including timed 100 squats at 50% of 1 rep max
Stanfa, 2017 [10]	34 collegiate swimmers at Midwest University; 13 diagnosed with ER[d]	Max pull-ups, rows, & bench presses for 2 complete cycles; tiebreaker round: repeat cycles or alt pushups & standing with arms held horizontal/perpendicular to floor
Tibana, 2018 [11]	Physically active 35-year-old female	Day 1 Session 1: 21 chest to bar pull ups, 21 thrusters, 9 chest to bar pull ups, 9 thrusters Session 2: 60 GHD[d] sit ups, 15 toes to bar Day 2 Session 1:1 RM[d] of squat snatch + overhead squat Session 2: AMRAP[d] 5 min of strict handstand push ups Session 3: 40 deadlifts, 20 kettlebells clean and jerks, 5 bar muscle ups

Footnotes:
[d] *CK* – creatine kinase, *ER* – exertional rhabdomyolysis, *GHD* – glutes-hamstring developer, *AMRAP* – as many rounds as possible, *RM* – repetition maximum

Similarly, in each case report individuals were diagnosed with exertional rhabdomyolysis after performing a workout that involved eccentric exercises. From the case reports analyzed (Figure 1), 44% were performing a combination of push-ups, pull-ups and/or dips, 32% were under military physical training, 16% performed squats and sled push/pulls and 8% engaged in high intensity interval training (HIIT). In the case reports, exertional rhabdomyolysis was diagnosed when individuals developed clinical symptoms leading them to seek medical care. Clinical symptoms included a common triad of myalgia, swelling and dark urine. Collectively 79 individuals reported symptoms with every individual reporting myalgias, 57 reporting dark urine, and 42 complaining of muscle swelling (Figure 2). During the medical evaluation, plasma CK levels were obtained with a suspicion of exertional rhabdomyolysis (Figure 3). Elevation of plasma CK above 15,000 U/L was found in each of the case reports. Smooth et al. reported a mean CK of 188,617 U/L, which was the highest mean CK of the case reports selected and particularly in the collegiate athletic setting. Oh et al. evaluated military case reports over a two-year span; the mean CK for the report was 84,725 U/L. In each of the case reports, the management of exertional rhabdomyolysis included administration of intravenous (IV) fluids and followed by discharge or hospitalization depending upon the clinical and laboratory severity of their condition. 78% of the case reports were admitted for treatment and observation while 22% were treated and discharged.

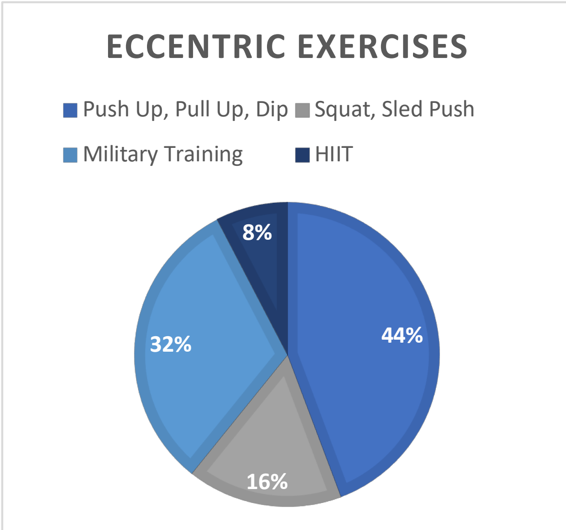

Figure 1 Case Reports: Types of Eccentric Exercises

Figure 2 Case Reports: Top 3 Symptoms Reported

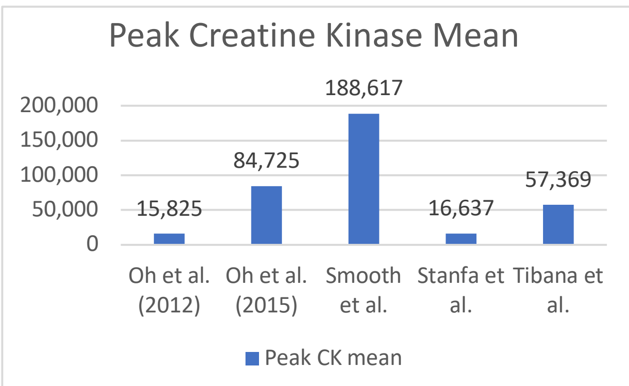

Figure 3 Case Reports: Mean CK Levels

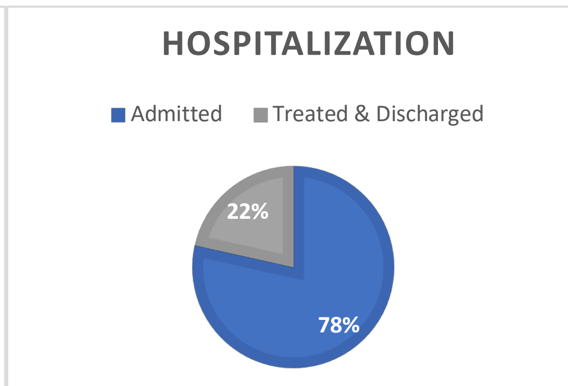

Figure 4 Case Reports: Management

Discussion:

An increase in the incidence of exertional rhabdomyolysis is profound given case reports found during this research. A PubMed search of exertional rhabdomyolysis in the past decade resulted in 52 case reports. These case reports examined various exertional rhabdomyolysis cause and effect. With limited primary literature available, a deeper understanding of the cause and effect of exertional rhabdomyolysis is open for interpretation. Case reports and available experimental trials are supportive of eccentric protocols being a major contributing factor to exertional rhabdomyolysis. Factors within an eccentric workout also play a role in the severity of exertional rhabdomyolysis. These factors include unaccustomed exercise, timed workouts and inadequate recovery time.

The research by Hody et al. supports the notion that eccentric based workouts have the potential to predispose a participant to exertional rhabdomyolysis. Given limited randomized control trials, further examination of eccentric exercises as a determinant of exertional rhabdomyolysis is scarce. Without more research on the condition, knowledge about predisposition factors of exertional rhabdomyolysis relies upon case reports. The case reports reviewed in this research had similarity among them with eccentric focused workouts. The workouts conducted included eccentric workouts where the focus was placed on strengthening muscles while in a lengthening load. These case reports demonstrate the concept that eccentric exercises may lead to exertional rhabdomyolysis when the workout is unaccustomed, timed or do not provide adequate recovery time. Case reports on exertional rhabdomyolysis have potential to increase as exercise competitiveness continues to rise.

With limited randomized control trials and research on the condition of exertional rhabdomyolysis, there are no guidelines encompassing the condition. Current recommendations addressing prevention, management and return to physical activity have been made based upon evidence from case reports. These guidelines are subjective and provide other areas within exertional rhabdomyolysis to be further examined. A section discussing management and treatment, return to physical activity and prevention strategies are discussed in the appendix of this paper. With limited research on determinants of exertional rhabdomyolysis, there is more importance on recognizing the condition, properly managing the effects, and understanding when to safely return an individual to physical activity. Guidelines in these areas are further explained in Appendix 1. Our understanding of exertional rhabdomyolysis currently comes from reported cases. More research surrounding the cause and effect of exercise protocols and exertional rhabdomyolysis will help medical providers and sport performance professionals develop productive, yet safer protocols.

Case reports of exertional rhabdomyolysis are increasing especially within controlled environments such as athletics. As the incidence continues to increase, hopefully an increase in research will follow. The case reports demonstrate how detrimental exertional rhabdomyolysis can be to one's health. Athletic case reports have begun to raise awareness of this condition leading to an open path for sport health researchers to further examine. Exertional rhabdomyolysis is no longer uncommon, and more research needs to be performed on this growing exercise health condition.

Conclusion:

Given the correlation in the increase of case studies and an increase in recognition and diagnoses of exertional rhabdomyolysis by medical providers, there is a growing amount of information on the topic. However, a gap in the research still remains because there are minimal randomized control trials assessing the impact of specific exercise regimens, including eccentric protocols, as well as various settings on the development of exertional rhabdomyolysis. The research presented in this paper points toward a causal relationship and has provided some evidence that eccentric exercise programs can increase the risk of developing exertional rhabdomyolysis. However, the research quality is limited to case reports with minimal randomized control trials leading the discussion that further research is warranted to determine the cause and effect of exertional rhabdomyolysis. The research presented in this paper can also assist health care professionals in identifying exertional rhabdomyolysis and providing treatment and management solutions. More research needs to be conducted to gain a better understanding of the condition and how to effectively educate sport performance professionals and medical providers to prevent future cases of exertional rhabdomyolysis.

Appendix

Appendix 1 - Management of Exertional Rhabdomyolysis:

Exertional rhabdomyolysis should always be suspected in patients whom have a history of recent exercise with complaints consistent with the signs and symptoms of the condition. Regardless of the physical status or level of exertion, exertional rhabdomyolysis should be considered. Given there are no published guidelines on management of exertional rhabdomyolysis, recommendations on treatment and return to sport activities are strongly based upon clinical judgement of the healthcare professional. Current research on exertional rhabdomyolysis is evolving leaving case reports as evidence for management of the condition.

Treatment

There are no available randomized controlled trials that offer evidence-based management for exertional rhabdomyolysis, specifically the decision of inpatient treatment versus close outpatient follow-up. Severity of patient symptoms and laboratory values of serum CK, potassium, BUN and creatinine should guide treatment decisions. The mainstay of treatment consists of aggressive IV hydration with isotonic 0.9% sodium chloride. Aggressive hydration assists with clearing toxic substances and increasing renal perfusion pressure thus preventing renal injury. The goal of IV hydration is to achieve a urine output of 200 to 300 mL/hour. In order to achieve the urine output goal, the isotonic 0.9% sodium chloride solution may need to be given at rate of one to two L/hour. Careful consideration should be given to patients who have comorbidities such as heart failure.[2]

Electrolyte abnormalities due to exertional rhabdomyolysis should also be monitored as part of the treatment plans. Hyperkalemia, hypocalcemia, hyperphosphatemia and hyperuricemia are common electrolyte abnormalities that are treated with standard therapy. Peritoneal dialysis or hemodialysis and a nephrology consult should be considered in patients with little or no output despite hydration, significant acute kidney injury, profound acidosis or severe hyperkalemia. Orthopedic surgery consult is recommended in a patient with suspected compartment syndrome.

Intravenous fluids are continued until the patient is well hydrated with normal serum electrolyte levels, normal renal function, and down-trending CK. The patient is then transitioned to oral hydration with recommendation to avoid strenuous activity until stabilized. Close follow-up within 24 to 48 hours is advised to monitor the patient's progress. Outpatient management for milder cases of exertional rhabdomyolysis consists of oral hydration with follow-up in 24 to 48 hours. [2]

Return to Sport Activities

Given the potential for severity with exertional rhabdomyolysis, return to physical activity should be closely monitored in order to prevent a relapse of the condition. Prior to resuming physical activity, blood and urine CK along with myoglobin levels should return to baseline for at least two to three days. Readiness is also assessed based on signs and symptoms, including muscle pain and discomfort. Guideline questions to consider before resuming activity are described in Table 6. The individual may resume mild physical activity under the supervision of a health care professional if all questions are answered 'yes'. Individuals who answer 'no' to any of the questions will need more time to allow their signs and symptoms to resolve.

Table 6 Guidelines for Provider: Return to Activity[8]

Return to Physical Activity Questions:
Is the individual afebrile?
Does the individual feel good (no flu-like symptoms)?
Is the individual well hydrated?
Are CK levels within normal limits?
Is myoglobin no longer present in serum and urine?
Is urine color clear or pale yellow, or less than four on a urine color chart?
Has muscle pain diminished to no pain?

An important factor in the recovery process is adequate hydration before, during and after physical activity. Adequate hydration and progression of physical activity is the baseline for return to physical activity. Literature provides health care professionals general guidelines for return to physical activity, but there are no published guidelines available. Health care professionals are advised to monitor blood and urine CK levels along with signs and symptoms to decrease the potential for reoccurrence. A safe return to physical activity is a combination of fluid replacement and a generalized conditioning program that is a mixture of aerobic and anaerobic training.

Cleary, et al. outlined a program with specific activities and recommendations on training-intensity (Appendix 2).[8] During the initial return to physical activity phase, eccentric exercise, downhill walking/running and weight lifting should be avoided. The initial phase focuses on a progression of intensity using the individual's tolerance as a guide. The protocol by Cleary et al. must be personalized, focusing on the individual's muscle injury, pre-incident level of fitness and previous weight lifting experience.[8] The suggested protocol is 15 weeks long and the intensity and duration of the program should be adjusted based upon the individual's needs, severity of injury and tolerance.[8]

Schleich, et al. a proposed 4-phase progressive program that focuses on returning athletes to sport without relapse of exertional rhabdomyolysis (Appendix 3).[9] Phase I includes daily monitoring of signs and symptoms such as muscle soreness, hydration status, urine characteristics, and uninterrupted sleep. Creatinine kinsase and serum creatinine were monitored by the team physician. Phase II continues daily monitoring of signs and symptoms with the addition of stretching and aquatic aerobic conditioning. Phase III builds on Phase II by adding body weight functional movement exercises and stationary cycling. Phase IV continues the progression and adds resistance training at 20-25% of estimated one-repetition maximum weight. The proposed program is a nine-week program that can be adjusted based upon athlete's severity of injury and conditioning status.[9]

Prevention Recommendations

Exertional rhabdomyolysis is a condition that can be prevented for those engaging in physical activity. With the guidance of health care professionals that are knowledgeable about the condition, these individuals are able to recognize potential signs and symptoms. Individuals conducting exercise programs should design a program geared toward moderation. The goal is to avoid too much, too soon, too fast. Group workouts can be motivating but risky because everyone is driven to work at the same pace and intensity. Conditioning status of those engaging in the program should be assessed with the knowledge that conditioning status does not a happen within a day but rather at a progression. Those with a low conditioning status should avoid high intensity workouts when being introduced or returning to a physical activity program.[1]

Another important key is communication about physical readiness and assessment for signs of physical distress in those who are partaking in physical activity. Hydration drives the human body in particular during exercise. Consumption of fluids should occur before, during and after physical activity to prevent possible dehydration. Individuals engaging in physical activity and particularly sport performance coaches conducting a workout should be mindful of exertional rhabdomyolysis and monitor for any potential signs and symptoms. "Workouts are meant to improve fitness, skills and athletic performance."[1] A successful training program is one that is a slow gradual progression that allows for recovery time and differences among individuals.

The National Collegiate Association of Athletics (NCAA) Handbook describes ten factors that can increase the risk of exertional rhabdomyolysis; these were lessons learned from previous team outbreaks (Table 7). With limited literature on exertional rhabdomyolysis, the lessons learned from prior cases provide the best insight onto the condition. With increased reported incidences of exertional rhabdomyolysis, the NCAA is attempting to be at the forefront providing guidance for this serious condition.

Table 7 NCAA Lessons from team outbreaks

Risk Factors for Exertional Rhabdomyolysis:
1. Athletes who try the hardest – give it their all to meet the demands of the coach (externally driven) or are considered the hardest workers (internally driven).
2. Workouts not part of a periodized, progressive performance enhancement program (e.g., workouts not part of the annual plan.
3. Novel workouts or exercises immediately following a transitional period (winter/spring break).
4. Irrationally intense workouts intended to punish or intimidate a team for perceived underperformance, or to foster discipline and "toughness."
5. Performing exercises to muscle failure during the eccentric phase of exercise such as repetitive squats (e.g the downward motion of squats) and then pushed beyond to continue.
6. Focusing a novel intense drill/exercise on one muscle with overload and fast repetitions to failure.
7. Increasing the number of exercise sets and reducing the time needed to finish (e.g. 100 squats, timed runs, station drills).
8. Increasing the amount of weight lifted as a percentage of body weight.
9. Trying to "condition" athletes into shape in a day or even over several days, especially with novel exercises or loads.
10. Conducting an unduly intense workout ad hoc after a game loss and/or perceived poor practice effort.

Weeks from Onset of ER	Recommended Activities and Environment Workout 5 days/week with no more than 2 days off between workouts (except Week 1)	Intensity	Precautions
Weeks 1-2	Aquatic exercise, swimming, walking, and jogging without equipment **Week 1**: workout 3 days **Week 2:** workout 5 days	60% HRR	Avoid eccentric activities, DH, WT, an exercise outdoors in warm/hot humid environment
Week 3	Aquatic exercises may begin to add hops and jumps and nonbuoyant resistance; increase intensity; begin eccentric with buoyant resistance	60 to 75% HRR	Begin some eccentric loading by adding buoyant resistance in water, avoid DH, WT, and exercise outdoors in warm/hot humid environment
Week 4	**Indoors in climate-controlled environment:** begin walking and running on a flat surface, followed by aquatic exercises **Outdoors in warm/hot humid environment:** no more than 20 minutes of continuous walking/running with progressive increase in intensity every 2 days	60 to 70% HRR on land 70 to 80% HRR in water	Avoid DH and WT; record BWT pre-and post-workout and rehydrate accordingly; shorts/shirts, no pads/equipment
Week 5	**Indoors in climate-controlled environment:** increase intensity of walking/running on flat surface, followed by aquatic exercises, 5 days/week **Outdoors in warm/hot humid environment:** no more than 30 minutes continuous walking/running with progressive increase in intensity every 2 days	70 to 80% HRR	Avoid DH and WT; record BWT pre-and post-workout; rehydrate accordingly/ shorts/shirts, no pads/equipment

Week 6	**Indoors in climate-controlled environment:** begin to introduce incline and decline walking/running, followed by aquatic exercise **Outdoors in warm/hot humid environment:** no more than 40 minutes, 10 minutes of interval training followed by 30 minutes of continuous walking/running with progressive increase in intensity every 2 days	60-80% HRR	Avoid DH and WT; record BWT pre-and post- workout; rehydrate accordingly; shorts/shirts; no pads/equipment
Week 7-8	**Indoors in climate-controlled environment:** introduce circuit WT program 3 days/week with one exercise per body area; walking and running all patterns, followed by aquatic exercise **Outdoors in warm/hot humid environment:** **Week 7:** no more than 50 minutes, 20 minutes of interval training followed by 30 minutes of continuous walking/running with progressive increase in intensity every 2 days **Week 8:** no more than 60 minutes, 10 minutes agility training, 20 minutes of interval training, followed by 30 minutes of continuous walking/running with progressive increase in intensity every 2 days	WT 50-67% of preinjury 1 RM HRR as required for sport	Progress slowly with WT; begin with 1 set of 10-15 reps to 3 sets by end of week 8 Avoid DH, record BWT pre-and post workout; rehydrate accordingly; shorts/shirts; no pads/equipment; water break every 20 minutes

Week 9-10	**Indoors in climate-controlled environment:** increase circuit WT program 3 days/week with 2 exercises per body area; walking and running all patterns, followed by aquatic exercise **Outdoors in warm/hot humid environment:** **Week 9:** no more than 70 minutes, 15 minutes agility training, 25 minutes of interval training followed by 30 minutes of continuous walking/running with progressive increase in intensity every 2 days **Week 10:** no more than 80 minutes, 20 minutes agility, 30 minutes of interval training followed by 30 minutes of continuous walking/running with progressive increase in intensity every 2 days	WT 65-75% of preinjury 1 RM HRR as required by sport	Progress slowly with weight training; begin with 1 set of 8-12 reps to 3 sets by end of 2nd week Record BWT pre- and post-workout; rehydrate accordingly; shorts/shirts, no pads/equipment; water break every 20 minutes
Week 11-12	**Indoors in climate-controlled environment:** increase circuit WT program 3 days/wk with 2-3 exercises per body area; walking and running all patterns, followed by aquatic exercise **Outdoors in warm/hot humid environment:** **Week 11:** 80 minutes, 20 minutes agility training, 30 minutes of interval training, followed by 30 minutes of continuous walking/running with progressive increase in intensity every 2 days **Week 12:** 80 minutes, 20 minutes agility training, 30 minutes of interval training followed by 30 minutes of continuous walking/running with progressive increase in intensity every 2 days	WT 75-85% of preinjury 1 RM HRR as required for sport	Progress slowly with weight training; begin with 1 set of 6-10 reps to 3 sets by end of 2nd week Record BWT pre-and post-workout; rehydrate accordingly. Wear pads 20-30 minutes, then remove for remainder workout

Week 13-14	**Indoors in climate-controlled environment:** continue circuit WT program as tolerated using aquatic exercise to prevent delayed onset of muscle soreness; may begin to add plyometric training **Outdoors in warm/hot humid environment: s**port specific practices and return to full practice with team (limited pads) or 80 minutes: 20 minutes agility training, 30 minutes interval training followed by 30 minutes of continuous walking/running with progressive increase in intensity every 2 days	HRR & WT, as required for sport	Continue slow progression in WT, plyometrics. Record BWT pre-and post-workout; rehydrate accordioning; wear pads for 60 to 80 minutes then remove for remainder of workout
Week 15	**Outdoors in warm/hot humid environment:** progress duration to length of practice that will be expected for return to play	70 to 85% HRR, as required by sport	Record BWT pre-and post-workout; rehydrate accordingly, water break every 20 minutes, wear pads for entire practice

Appendix 2 Progression of Activity Following Rhabdomyolysis with Environmental Acclimatization[8]

HRR: heart rate reserve, DH: downhill walking/running, WT: weight training, RM: repetition maximum, BWT: body weight; Rehydrate with same volume of fluid lost as body weight changes. Interval training should include a work to rest interval equal or 1:1 allowing athlete to train at near maximum level for greater amount of time

Phase	Activities
I	Return to activities of daily living for 2 week Regular monitoring by athletic training staff Screening for symptoms consistent with exertional rhabdomyolysis, sleep patterns, hydration, urine color, and class attendance Monitoring of creatinine kinase and serum creatinine by PCP
II	Daily monitoring of hydration status, muscle soreness, and swelling Initiation of physical activity: foam rolling, dynamic warm-up, aquatic jogging, and stretching
III	Daily monitoring of hydration status, muscle soreness, and swelling Progression of physical activity: body weight resistance movements, resistance training with elastic band, core training stationary bicycling, and stretching
IV	Daily monitoring of hydration status, muscle soreness, and swelling Initiation of resistance training at 20-25% of estimated 1-repetition maximum, agility exercises, and running

Appendix 3 Overview of Phased Return[9]

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