

Exertional Rhabdomyolysis: Determining Readiness to Return to Play

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KEY POINTS

▶ Myoglobin may be an appropriate biochemical marker for determination of readiness to return to activity following a diagnosis of exertional rhabdomyolysis.

▶ Return to play should be individualized, and biochemical markers should not be exclusively relied upon to assess an athlete's status.

▶ Return to play should be progressive and should include hydration monitoring and acclimatization.

Exertional rhabdomyolysis results from muscle tissue breakdown, which presents a significant concern for the possibility of renal failure.¹⁻⁵ Athletic trainers and therapists (ATs) need to be knowledgeable about its prevention and treatment, as well as considerations for safe return to activity. Rhabdomyolysis is diagnosed on the basis of elevation of serum creatine kinase (CK) and myoglobin (Mb).⁶⁻¹⁶ The same biological markers can be used to assess readiness for return to activity, but much of the available literature on the topic has focused on serum CK level as the basis for the decision.^{1,11-13,16-20} There is research evidence, however, that serum Mb may be a more sensitive indicator of physiologic status.^{6-10,14,15} The purpose of this report is to review the evidence for use of Mb as a more sensitive marker for making a return-to-play decision after exertional rhabdomyolysis has been diagnosed.

Pathogenesis

Exertional rhabdomyolysis results from insufficient synthesis of adenosine triphosphate

(ATP) to meet energy demands, which is typically associated with excessive muscular activity, temperature extremes, and muscle ischemia.⁶ Cell destruction caused by rhabdomyolysis occurs much faster in extreme heat,⁶ which has been associated with muscle in military personnel, football players, and individuals participating in intense physical activity (Figure 1).^{1,2,17,19,21-24}

Rhabdomyolysis involves disruption of the sarcolemma and intracellular structural components.^{3-5,16} Hypoxia, ATP depletion, and alteration of sodium-potassium electrolyte balance may contribute to increased

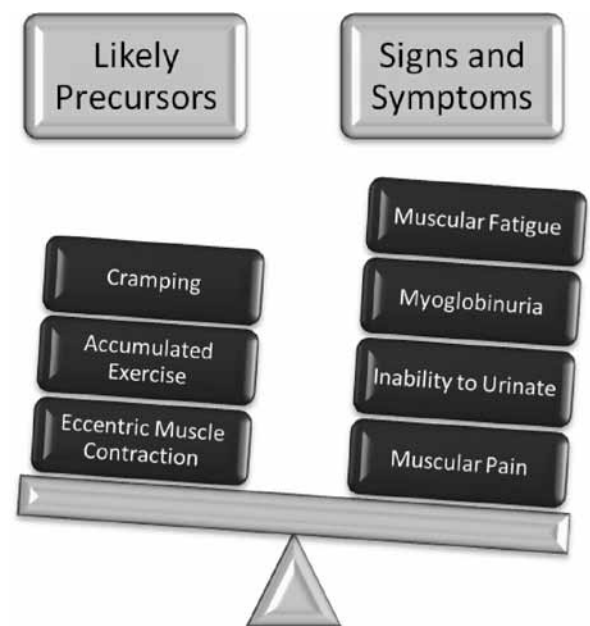


Figure 1 Likely precursors, clinical signs and symptoms of exertional rhabdomyolysis.

serum CK and Mb levels.^{3-5,16} Excessive serum CK and Mb levels can lead to kidney failure and death when untreated,^{3-5,16} but a catastrophic outcome is unlikely.²⁵ Some physicians may use CK as the only biological marker for the diagnosis of exertional rhabdomyolysis and for subsequent assessment of readiness for return to play.^{1,11-13,16-20} There is a body of evidence, however, that supports the use of Mb as a biological marker for evaluation of physiologic status.⁶⁻¹⁰

Biochemical Markers

Serum CK levels vary between physically fit athletes and sedentary individuals. The range of normative values observed in the general population may not include levels measured in highly trained athletes who are in a constant state of muscle rebuilding.^{6,7} Because athletes can have resting serum CK levels that are substantially greater than those for untrained individuals,²⁵ physician use of normative values derived from the general population may adversely affect diagnostic accuracy and probably should not be used for assessment of readiness to return to play (Table 1).^{13,26,27} Untrained individuals will also exhibit greater increase in serum CK levels than athletes during fatiguing activity.^{12,28,29} The presence of an appreciable quantity of Mb in the serum is abnormal for anyone (abnormal values range from 4.5 to 37.5ug/ml).¹⁰

Research has demonstrated that CK level does not accurately predict renal failure, but a serum Mb level above 1000 ng/ml does appear to relate to renal failure.^{9,30} Dark cola-colored urine, commonly associated with rhabdomyolysis, does not occur unless urine myoglobin levels exceed 100 mg/dL.¹⁶ A possible reason for variability in CK level is transport of the large CK molecule through the lymphatic system, which delays serum CK peak until 96 to 120 hours postexercise or postinjury.⁷ Mb is a much smaller molecule that is readily transported within the vascular system, which allows for a more rapid serum Mb peak at 24 to 72 hours postexercise or postinjury.⁷

Variability in CK levels are also influenced by gender, ethnicity, and environmental temperature. CK levels tend to be higher in individuals who participate in cold weather activities.^{12,28,29} Females typically have lower CK levels than males do,¹¹ which is an important factor to consider when reviewing published case studies. The literature contains 15 case studies on exertional rhabdomyolysis in male athletes and military personnel, but none report cases involving female patients.^{1,2,17,19,21-24} CK levels could be assessed as part of a preparticipation physical examination, but the cost of testing may be prohibitive.¹¹ Lacking baseline serum CK data, and considering the variability in serum CK levels, serum Mb level may provide a better indicator of readiness to return to play.¹⁴

Return to Activity

A clearly-defined standard for return to play following a diagnosis of exertional rhabdomyolysis is not available in the literature. Return to activity ranges from none (i.e., mortality) to one month following symptom onset (Table 2). One case study has recommended a 15-week return to play progression, but the case reported involved a return to play within seven days.²³ No timeline for follow-up evaluation of biological markers related to exertional rhabdomyolysis has been established.²³ Therefore, the following guidelines are recommended for the return to play of athletes who have been diagnosed with exertional rhabdomyolysis.

1. Return to activity should be individualized. Because rhabdomyolysis often occurs in individuals who have other concomitant conditions,^{1,2,17,19,21-24} numerous variables may play a role in determination of an appropriate timeline for return to activ-

TABLE 1. SERUM BIOLOGICAL MARKERS FOR DIAGNOSIS AND RETURN TO ACTIVITY IN PATIENTS WITH RHABDOMYOLYSIS

| Biological Marker (serum) | Normal Range* | Half Life or Dissolution Rate ^B |
|---------------------------|--|---|
| Creatine Kinase (CK) | 45 – 260 IU/L ¹³ 32 – 267 IU/L ²⁶ Male 30 – 220 IU/L ²⁷ Female 20 – 170 IU/L ²⁷ | Presentation 12 hr Peaks 2 – 3 days Decline 3 – 5 days Half Life: 1.5 days |
| Myoglobin (Mb) | 80 ng/mL ¹³ 0 – 12 IU/L ²⁶ 0 – 16 IU/L ²⁷ | Presentation 4 hr post infarction Decline 6 – 8 hours Half Life: 2 – 3 hours |

*Normal ranges are as much dictated by historical texts and medical literature as they are by manufacturers and laboratories. We have provided norms from current and reputable research; however, clinicians should regard the information provided by the overseeing physician and laboratory as well as the information provided in this text.

TABLE 2. RETURN TO ACTIVITY ARTICULATED IN THE LITERATURE

| Author | Return to Activity Parameters |
|---|--|
| Anzalone et al. (2010) ² | Case: 19 y/o African American male football player with sickle cell trait experiences exercise associated collapse after weight lifting and sprint workout RTA: none (fatal within 15 hr of incident) |
| Moeckel-Cole et al. (2009) ¹ | Case: 18 y/o male football player (placekicker) reported to emergency room 24 hr following eccentric conditioning practice RTA: discharged @ 8 days; returned unrestricted to football activities at 1 month |
| Mrsic et al. (2008) ¹⁷ | Case: patient with coma following heroin and alcohol consumption results in muscular compression injury leading to acute compartment syndrome RTA: surgical intervention required (multiple fasciotomy procedures and debridement); discharged after 6 weeks |
| Cleary et al. (2007) ²³ | Case: 16 y/o Hispanic male football player with full body muscle cramping after full football practice and sprint workout in extreme heat RTA: returned to unrestricted football activities within 7 days; complimented normal fluid replacement during practice with a 16 oz carbohydrate-electrolyte solution pre and post practice for 2 weeks |
| Dincer et al. (2005) ²⁴ | Case: 31 y/o African American male in military training with sickle cell trait experiences multiple compartment syndrome after a 5-mile run RTA: none (surgical intervention failed and patient died within 8 hours) |
| Kuklo et al. (2000) ²² | Case: 33 y/o African American male experiences exercise associated collapse after a timed 2-mile run during a semiannual U.S. Army Physical Fitness Test RTA: none (fatal) |
| Gardner et al. (1994) ²¹ | Case: 30 y/o African American male with sickle cell trait presents with afebrile heat exhaustion RTA: none (fatal) |
| Kodama et al. (1985) ¹⁹ | Case: 23 y/o Japanese male in military training with aldosteronism after heat exhaustion with hypertonic dehydration RTA: regained consciousness after 15 d; serum CPK returned to normal after 30 days, just one day following his first day of standing unaided |

ity. Graduated and monitored return is best, and activities should be tailored to the athlete and sport.

2. Although impractical to obtain, a baseline serum CK level would be needed to properly use serum CK level as criterion for return to play.¹¹ CK and Mb are both involved in the pathogenesis of rhabdomyolysis.³⁻⁵ CK elevation lingers long after the symptoms of the condition subside.¹³ Mb is cleared by the kidneys in a much shorter time, however.¹³ Return to activity may be appropriate when the patient demonstrates normal serum and urine Mb levels and he or she no longer experiences muscle pain and/or fatigue and myoglobinuria (reddish-brown urine). Patients should be progressively returned to activity, because “normal” serum and urine Mb levels can vary for individuals.¹¹
3. Acclimatization is essential,²³ particularly for athletes returning to intense participation of training

in a hot and humid environment. These are times during the training cycle when the condition may be more likely to develop (i.e., psychosocial aspects of sport can influence motivation and zealously).

4. ATs should monitor hydration status before, during, and after exercise sessions. A thorough assessment should include urine specific gravity, urine color, and change in body mass.^{31,32} To customize hydration monitoring, sweat rate can be calculated, and fluid replacement should match the volume of fluid lost. Although hypohydration is not always concomitant with rhabdomyolysis, several case reports have linked these conditions.^{1,2,17,19,21-24}
5. Evidence of muscle fasciculation should result in complete cessation of activity, especially when a recurrent mechanism of injury is exhibited. Eccentric muscle loading should also be avoided during the early stages of return to activity, because it may

produce rapid muscle fatigue. Stretching, cryotherapy, massage, and electrolyte replacement are the most common treatments for exercise-associated muscle cramps,^{31,32} which are sometimes associated with the onset of exertional rhabdomyolysis.^{1,2,17,19,21-24}

Conclusions

Although the literature has emphasized CK level as the most sensitive biochemical marker for the diagnosis of rhabdomyolysis, several factors influence its presence in serum. Individual variability in serum CK level can complicate the diagnosis of exertional rhabdomyolysis and may preclude its use as a criterion for determination of readiness for return to activity. Mb is quickly removed from serum (i.e., shorter half-life than CK), which may make serum Mb level a better indicator of the body's response to muscle cell damage than serum CK level. Exclusive reliance on serum CK level as a biological marker of physiologic status after a diagnosis of exertional rhabdomyolysis may unnecessarily prolong return to activity. ■

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