How much can exercise raise creatine kinase level—and does it matter?

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Evidence-based answer

Moderate-intensity exercise (maintaining heart rate between 55% and 90% of maximum) may elevate creatine kinase (CK) to levels that meet the diagnostic criteria for rhabdomyolysis if the exercises involve eccentric muscle contractions, such as weight lifting or downhill running (strength of recommendation [SOR]: **C**, small observational studies). The clinical significance of exercise-induced elevations in CK is unclear because the renal complications associated with classic rhabdomyolysis haven't been observed.

Clinical commentary

Be vigilant, but not hypervigilant

Elevated CK noted on incidental testing can be vexing for physicians who treat athletes. Because asymptomatic exertional rhabdomyolysis is historically underdiagnosed and underappreciated, one may feel compelled to test all such patients for renal function, electrolytes, and myoglobinuria.[1]

Vigilance is mandatory—especially for symptoms of myalgia, generalized weakness, and dark urine—but this Clinical Inquiry also supports using a sound patient history and clinical judgment to avoid extensive laboratory testing or hospital admission. Indeed, patients who participate in moderate intensity, eccentric muscle contraction activities can be followed as outpatients because a correlation between CK elevation and renal dysfunction has not been detected in this group.

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FAST TRACK

Use a sound patient history and clinical judgment to avoid extensive laboratory testing and hospital readmission

Evidence summary

Rhabdomyolysis is a well-described clinical syndrome resulting from injury to skeletal muscle and subsequent release of cellular contents into the extracellular fluid and circulation. It can lead to many complications, including renal failure, disseminated intravascular coagulation, and even death in 5% of cases.[2] The leading causes of rhabdomyolysis include trauma, soft tissue compression, alcohol, drugs, infections, seizures, and exercise.[3]

Only half of patients experience muscle pain.[2] Elevations occur in multiple serum markers, including CK, myoglobin, aldolase, lactate dehydrogenase, alanine aminotransferase, and aspartate aminotransferase, in either plasma or urine.[4,5]

Variable elevations, ranging from mild to extreme, that are discovered incidentally after exercise may cause clinical uncertainty.

CONTINUED

FAST TRACK

Triathletes had a 12-fold mean increase in CK levels as long as 24 hours after a race

No clear consensus defines CK levels in rhabdomyolysis

CK is the primary serum marker for rhabdomyolysis. It's highly sensitive, but not specific. No clear consensus exists on what threshold of CK elevation correlates with clinically relevant disease.[6] A relationship between CK elevation and the severity of disease has been established (>6000 IU/L predicts renal failure), but patients can have significant morbidity with only moderately elevated CK levels.[7,8] Normal reference ranges for serum CK are 55 to 170 IU/L for males, and 30 to 135 IU/L for females.[9]

Recent definitions of rhabdomyolysis have been established to address muscle toxicity from lipid-lowering medications. The United States Food and Drug Administration specifies a CK level of more than 50 times the upper limit of normal (ULN)—or 10,000 IU/L—accompanied by organ damage, usually renal compromise.[6] The National Lipid Association's Muscle Safety Expert Panel has defined rhabdomyolysis as any evidence of muscle cell destruction regardless of the CK level and a causal relationship to a change in renal function. The panel further subdivides CK elevations into categories of mild (<10 times ULN), moderate (10-49 times ULN), and marked (≥50 times ULN).[6]

Exercise elevates CK level, but consider other factors, too

Although exercise is known to elevate CK, it produces a wide range of levels, based on a host of variables.[3,10] Increases in CK are more pronounced in males, blacks, and untrained people; age doesn't seem to be a factor.[10,11] Higher-intensity, longer-duration, and weight-bearing exercise (eccentric muscular contractions and downhill running) cause the greatest rises in CK.[10] Other influences include temperature, altitude, gravitational forces, noise, and vibration.

No studies firmly establish a normal range of CK elevation from moderate exercise; better data are available for extreme athletes, such as long-distance runners and triathletes. One study found that mean total CK elevations 24 hours after a marathon were 3322 IU/L (22.3 times baseline) for men and 946 IU/L (8.6 times baseline) for women.[4] Another study showed that triathletes had a 12-fold mean increase in CK levels as long as 24 hours after the race.[12]

Eccentric exercises significantly raise CK

Exercise programs that include eccentric muscle contractions can result in significant serum CK elevations. One study followed 203 participants to evaluate the magnitude of CK elevation and the effect on renal function produced by exercise.[3] After performing 50 maximal eccentric elbow flexor contractions, 55% of participants had CK elevations >2000 IU/L at 4 days after exercise; 25% had CK elevations >10,000 IU/L; 13% had levels >20,000 IU/L. None showed any evidence of renal compromise on clinical follow-up. Another study found significant increases in CK (approximate mean of 15,000 IU/L) after repetitive eccentric elbow flexor contractions in college-age males.[13]

Eccentric weight lifting and similar activities, like downhill running, may result in an increase in serum CK levels of 10 to 20 times normal, whereas other nonweight-bearing exercises and exercise involving no or minimal eccentric contractions, such as swimming and cycling, cause only nominal increases in serum CK.[10]

Recommendations

No formal guidelines from authoritative sources are available. ■

Acknowledgments

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