Creatine kinase, CK

Pseudonyms: Total CK, adenosine triphosphate:creatine N -phosphotransferase (EC 2.7.3.2), creatine phosphokinase, phospho-creatine kinase

General information

Creatine kinase (CK) is a dimeric enzyme that catalyses the reversible phosphorylation of creatine by ATP. CK is released into blood following damage to muscle tissue, resulting in elevated serum/plasma CK activity.

CK is composed of two subunits, M and B, which form three different active complexes: CK-BB, CK-MB and CK-MM. CK-MM is predominantly found in striated muscle and heart tissue, whereas CK-BB is predominantly found in brain tissue and smooth muscle. CK-MB is more specific for heart muscle. Routine measurement of CK activity measures all three isoenzymes (total CK). Measurement of CK-MB for the investigation of myocardial infarction has largely been superseded by troponin T.
CK is the most sensitive serum marker for muscle damage and can be elevated in any condition that causes muscle injury. It is routinely used in the evaluation of patients with suspected myopathy (e.g. patients presenting with unexplained muscle weakness or myalgia), and the investigations of myositides and suspected rhabdomyolysis. It can also be used to monitor disease course.

Baseline measurement of CK is also recommended in patients with familial hypercholesterolaemia prior to initiation of statin therapy (NICE Clinical Guideline CG71). Routine monitoring of CK in asymptomatic patients is not recommended. However, if patients become symptomatic (muscle pain and weakness), urgent CK measurement is recommended (2016 ESC/EAS Guidelines for the Management of Dyslipidaemias).

Collection container
Adults - serum (with gel separator, 4.9mL Sarstedt brown top).
Paediatrics - lithium heparin plasma (1.2mL Sarstedt orange top tube)

Type and volume of sample
Serum or lithium heparin plasma, minimum 1ml whole blood required (200 µl separated serum/plasma).

Specimen transport/special precautions: No special precautions required

Laboratory information

Method principle:
Automated enzymatic colorimetric assay (Roche cobas platform)
Creatine phosphate + ADP → (CK) → creatine + ATP
ATP + D-glucose → (hexokinase) → ADP + glucose-6-phosphate (G6P)
G6P + NADP+ → (G6P dehydrogenase) → D-6-phosphogluconate + NADPH + H+
The production of NADPH is proportional to GGT activity in the sample and is determined spectrophotometrically by the increase in absorbance at 340 nm.

Biological reference range or cut off:

Up to 2 weeks		10-600 IU/L
2 weeks up to 1 month		< 400 IU/L
1 month up to 1 year		< 300 IU/L
> 1 year	Male	40-320 IU/L
	Female	25-200 IU/L

Turnaround time: Results are available within 2 hours (urgent - phone lab in advance of sampling) or 4 hours (routine).

Clinical information

Serum CK activity is increased when damage of any cause occurs to skeletal or heart muscle. Very high levels can be seen in all types of muscular dystrophy, crush injuries/rhabdomyolysis, burns, viral myositis, polymyositis, and other inflammatory myopathies. In Duchenne and Becker muscular dystrophy, CK levels are typically elevated from the newborn period, prior to clinical presentation.

Note CK is a more sensitive marker of rhabdomyolysis and a better predictor of acute kidney injury than urine myoglobin in patients with rhabdomyolysis due to trauma or burns.

Elevated serum CK is also associated with various drug-induced myopathies, including colchicine, anti-malarials, statins, cocaine and alcohol.

Clinical decision limits: The 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias recommend re-evaluation of indication for statin treatment if CK becomes elevated ≥ 4 x upper limit of normal (ULN). If > 10 x ULN, treatment should be stopped.

Factors known to significantly affect the results: Reference ranges quoted above are based on studies in Caucasians, higher values are observed in black populations. CK can be significantly elevated by strenuous exercise.

Non-pathological elevations of CK activity can rarely be observed due to the formation of macromolecular forms of the enzyme, termed macro-CK. If suspected, samples can be sent for macro-CK identification by electrophoresis.

References:

1) Rifai N, Horvath AR, Wittwer CT. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 6th Edition. Elsevier.
2) Miller M. Muscle enzymes in the evaluation of neuromuscular diseases (UpToDate; accessed October 2018)
3) NICE Clinical Guideline CG71. Familial hypercholesterolaemia: identification and management
4) The Task Force for the Management of Dyslipidaemias of the ESC and EAS. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias. European Heart Journal (2016) 37, 2999–3058.