Approach to a patient with elevated CK

Lee Liou, M.D., Ph.D.
Swedish Neuroscience Institute
Disclosures

None
Outline

- Creatine kinase biochemistry
- Normal values
- Factors which can affect CK levels
- CK as a biomarker for muscle disease
- Approach to a patient with elevated CK
- Asymptomatic elevations in CK
Creatine Kinase Biochemistry
Phosphocreatine System

- Used by tissues that have high demand for energy
  - Skeletal muscle
  - Cardiac muscle
  - Brain tissue
- Creatine is used as a buffer to store energy which is easily converted to ATP
  - ATP concentration in muscle is 2-5 mM
  - Creatine concentration in muscle is 20-40 mM
Phosphocreatine System

Creatine Kinase

- Catalyzes the transfer of a high energy phosphate between ATP and creatine
- Functions as a dimer
- Two subunit types
  - M type
  - B type
Creatine Kinase

- Tissue isoforms
  - Skeletal muscle
    - 2 M subunits (MM)
  - Brain
    - 2 B subunits (BB)
  - Cardiac muscle
    - One of each (MB)
Laboratory Testing

- Total CK
  - Assay based on enzyme activity
    - One unit of activity is defined as the transfer 1 micromole of phosphate from phosphocreatine to ADP per minute
  - Laboratory reference is U/L

- CK-MB
  - Assay to quantitate amount of protein using a specific antibody to CK-MB
  - Laboratory reference is ng/mL
What is normal?
What is normal?

- Normal laboratory reference ranges are typically defined as the interval containing 95% of reference population.
- The “reference population” may not accurately reflect your patient population.
- Laboratory normal ranges typically assume Gaussian distribution.
What is normal?

- Total CK
  - Swedish lab
    - Male: 24-204 U/L
    - Female: 24-173 U/L
  - UW lab
    - Male: 62-325 U/L
    - Female: 43-274 U/L
  - Mayo Clinic lab
    - Male: 52-336 U/L
    - Female: 38-176 U/L
Creatine Kinase

- Creatine kinase levels are non-Gaussian

Creatine Kinase (Netherlands)

Study with 1411 subjects

<table>
<thead>
<tr>
<th>Sex and ancestry</th>
<th>N</th>
<th>Age (SD)</th>
<th>BMI (SD)</th>
<th>2.5th percentile</th>
<th>Median</th>
<th>97.5th percentile</th>
<th>&gt;ULN (N%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td>1411</td>
<td>45 (7)</td>
<td>27 (5)</td>
<td>40</td>
<td>111</td>
<td>460</td>
<td>508 (36)</td>
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<tr>
<td>Women</td>
<td>831</td>
<td>45 (7)</td>
<td>28 (6)</td>
<td>36</td>
<td>95</td>
<td>349</td>
<td>304 (37)</td>
</tr>
<tr>
<td>Men</td>
<td>580</td>
<td>46 (7)</td>
<td>26 (4)</td>
<td>51</td>
<td>143</td>
<td>616</td>
<td>204 (35)</td>
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<tr>
<td>White subjects</td>
<td>503</td>
<td>48 (7)</td>
<td>26 (5)</td>
<td>35</td>
<td>88</td>
<td>286</td>
<td>64 (13)</td>
</tr>
<tr>
<td>Women</td>
<td>252</td>
<td>47 (7)</td>
<td>26 (5)</td>
<td>29</td>
<td>72</td>
<td>201</td>
<td>21 (8)</td>
</tr>
<tr>
<td>Men</td>
<td>251</td>
<td>48 (7)</td>
<td>26 (4)</td>
<td>47</td>
<td>110</td>
<td>322</td>
<td>43 (17)</td>
</tr>
<tr>
<td>South Asian</td>
<td>270</td>
<td>44 (6)</td>
<td>27 (5)</td>
<td>40</td>
<td>104</td>
<td>382</td>
<td>62 (23)</td>
</tr>
<tr>
<td>Women</td>
<td>147</td>
<td>45 (6)</td>
<td>27 (5)</td>
<td>37</td>
<td>87</td>
<td>313</td>
<td>23 (16)</td>
</tr>
<tr>
<td>Men</td>
<td>123</td>
<td>44 (6)</td>
<td>26 (5)</td>
<td>47</td>
<td>143</td>
<td>641</td>
<td>39 (32)</td>
</tr>
<tr>
<td>Black subjects</td>
<td>570</td>
<td>44 (6)</td>
<td>28 (5)</td>
<td>51</td>
<td>149</td>
<td>627</td>
<td>278 (49)</td>
</tr>
<tr>
<td>Women</td>
<td>387</td>
<td>43 (6)</td>
<td>29 (6)</td>
<td>48</td>
<td>124</td>
<td>414</td>
<td>164 (42)</td>
</tr>
<tr>
<td>Men</td>
<td>183</td>
<td>44 (6)</td>
<td>26 (4)</td>
<td>71</td>
<td>213</td>
<td>801</td>
<td>114 (62)</td>
</tr>
</tbody>
</table>

Data for age and body mass index (BMI) are means (SD). Data are rounded to the nearest integer. CK is expressed as international units per liter.

*Number (percentage) of participants with a CK above the ULN, as recommended by the manufacturer (140 IU/L for women, 174 IU/L for men; with appropriately established reference intervals, 2.5% of the subjects are expected to have values above the ULN).

(North of participants of “other” ancestry (n = 68), with the exclusion of outliers (n = 3, 1 South Asian and 2 black participants) and those using statins (n = 30, 21 South Asian, 8 black participants, and 1 of other ancestry)."

## Creatine Kinase in the US

George et al. Medicine (2016) 95:33

<table>
<thead>
<tr>
<th>Characteristics of NHANES subjects 2011–2014, age ≥ 20, nonpregnant, with available creatine kinase</th>
<th>N=10,096</th>
<th>Average CK 102</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>10,096</td>
<td></td>
</tr>
<tr>
<td>Race-ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>4119 (41%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>2256 (22%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>2159 (21%)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>1270 (13%)</td>
<td></td>
</tr>
<tr>
<td>Other race*</td>
<td>292 (3%)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>1686 (17%)</td>
<td></td>
</tr>
<tr>
<td>30–49</td>
<td>3514 (35%)</td>
<td></td>
</tr>
<tr>
<td>50–69</td>
<td>3340 (33%)</td>
<td></td>
</tr>
<tr>
<td>≥70</td>
<td>1556 (15%)</td>
<td></td>
</tr>
<tr>
<td>Survey year</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2011–2012</td>
<td>4833 (48%)</td>
<td></td>
</tr>
<tr>
<td>2013–2014</td>
<td>5263 (52%)</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29 ± 7</td>
<td></td>
</tr>
<tr>
<td>Glomerular filtration rate, mL/min/1.73 m²</td>
<td>89 ± 26</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>3616 (36%)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>2038 (20%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1586 (16%)</td>
<td></td>
</tr>
<tr>
<td>Cholesterol medication use</td>
<td>1973 (20%)</td>
<td></td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>719 (7%)</td>
<td></td>
</tr>
<tr>
<td>Vigorous work</td>
<td>1738 (17%)</td>
<td></td>
</tr>
<tr>
<td>Vigorous recreation</td>
<td>2243 (22%)</td>
<td></td>
</tr>
<tr>
<td>Exercise past 3 days (n=4331)</td>
<td>1086 (25%)</td>
<td></td>
</tr>
<tr>
<td>Heavy alcohol use (n=4386)*</td>
<td>355 (8%)</td>
<td></td>
</tr>
<tr>
<td>Creative kinase, IU/L</td>
<td>102 (72, 158)</td>
<td></td>
</tr>
</tbody>
</table>
Creatine Kinase in the US

George et al. Medicine (2016) 95:33
Creatine Kinase in the US

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>90th percentile</td>
</tr>
<tr>
<td>White</td>
<td>532</td>
<td>237 (201,273)</td>
</tr>
<tr>
<td>Black</td>
<td>391</td>
<td>544 (443,645)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>304</td>
<td>274 (234,314)</td>
</tr>
<tr>
<td>Asian</td>
<td>214</td>
<td>267 (188,346)</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>90th percentile</td>
</tr>
<tr>
<td>White</td>
<td>655</td>
<td>142 (130,154)</td>
</tr>
<tr>
<td>Black</td>
<td>485</td>
<td>254 (205,303)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>359</td>
<td>145 (124,166)</td>
</tr>
<tr>
<td>Asian</td>
<td>216</td>
<td>135 (120,150)</td>
</tr>
</tbody>
</table>

CK = creatine kinase, NHANES = National Health and Nutrition Examination Survey.

George et al. Medicine (2016) 95:33
What factors affect the CK level?
Exercise

Effect of 3 days of 45 min aerobic exercise sessions on 15 medical students

<table>
<thead>
<tr>
<th>Subject</th>
<th>Days after exercise</th>
<th>Serum CK (U/L)</th>
<th>Muscle pain (day)</th>
<th>Mean recovery pulse (beats/min)</th>
<th>CK ratio (peak/resting)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>1†</td>
<td>204</td>
<td>363</td>
<td>—</td>
<td>—</td>
<td>149</td>
</tr>
<tr>
<td>2†</td>
<td>232</td>
<td>147</td>
<td>87</td>
<td>31</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>472</td>
<td>—</td>
<td>103</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>256</td>
<td>152</td>
<td>103</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>392</td>
<td>234</td>
<td>184</td>
<td>117</td>
<td>67</td>
</tr>
<tr>
<td>6</td>
<td>546</td>
<td>428</td>
<td>—</td>
<td>171</td>
<td>—</td>
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<tr>
<td>7</td>
<td>103</td>
<td>58</td>
<td>—</td>
<td>59</td>
<td>53</td>
</tr>
<tr>
<td>8</td>
<td>282</td>
<td>173</td>
<td>162</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>3473</td>
<td>3465</td>
<td>911</td>
<td>408</td>
<td>99</td>
</tr>
<tr>
<td>10</td>
<td>264</td>
<td>121</td>
<td>90</td>
<td>127</td>
<td>—</td>
</tr>
<tr>
<td>11</td>
<td>90</td>
<td>50</td>
<td>44</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>12</td>
<td>164</td>
<td>110</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>13</td>
<td>—</td>
<td>1458</td>
<td>—</td>
<td>140</td>
<td>48</td>
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<tr>
<td>14</td>
<td>178</td>
<td>121</td>
<td>—</td>
<td>89</td>
<td>—</td>
</tr>
<tr>
<td>15*</td>
<td>692 (379)</td>
<td>689 (235)</td>
<td>532</td>
<td>325</td>
<td>174</td>
</tr>
<tr>
<td>Mean</td>
<td>73.87</td>
<td>31.12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>31.12</td>
<td>10.77</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*This subject was the aerobics instructor who was carrying out three classes per week. The values shown are the values obtained when she first began classes. Values in parentheses are the values obtained while giving this test program.
†Subjects 1 and 2 carried out regular exercise at least 3 times per week. Subject 1 jogged for 40 minutes 2–3 times per week and played netball twice per week. Subject 2 cycled 5 km to the hospital and attended gymnastics twice per week. She was also taking propranolol for hypertension.
‡Days −3, −2, −1 were the 3 aerobic exercise days, days 1–7 were days following the aerobic exercise.
§Resting serum CK values were obtained from the mean of a minimum of three serum CK values obtained at weekly intervals, using the collection protocol described in Materials and Methods.
Exercise

Study of 499 recruits undergoing basic military training

<table>
<thead>
<tr>
<th>Race</th>
<th>Number</th>
<th>Baseline CK, mean/median (P-value)</th>
<th>Day 7 CK, mean/median (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>African-American</td>
<td>27</td>
<td>664.4/371.5</td>
<td>2762.1/1548.0</td>
</tr>
<tr>
<td>Asian</td>
<td>8</td>
<td>351.0/247.5 (0.220)</td>
<td>1563.0/529.0 (0.141)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>379</td>
<td>186.8/152.0 (&lt;0.001)</td>
<td>1184.1/555.0 (&lt;0.001)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>57</td>
<td>260.4/153.0 (&lt;0.001)</td>
<td>1070.0/533.0 (&lt;0.001)</td>
</tr>
<tr>
<td>Native American</td>
<td>9</td>
<td>233.6/183.0 (0.015)</td>
<td>1006.5/961.5 (0.054)</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>15</td>
<td>171.3/118.0 (&lt;0.001)</td>
<td>695.0/387.5 (&lt;0.001)</td>
</tr>
</tbody>
</table>

P-values (two-tailed) are with respect to the log of serum CK, with all comparisons made vs. African-Americans. Bold = statistically significant at P < 0.05.

Exercise

Study of 499 recruits undergoing basic military training

<table>
<thead>
<tr>
<th>Table 1. Mean serum CK values at baseline, and at days 3, 7, and 14 after starting BMT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>CK</td>
</tr>
<tr>
<td>Mean (IU/L)</td>
</tr>
<tr>
<td>Range</td>
</tr>
<tr>
<td>Median (IU/L)</td>
</tr>
<tr>
<td>Abnormal</td>
</tr>
<tr>
<td>&gt;5× normal</td>
</tr>
<tr>
<td>&gt;10× normal</td>
</tr>
<tr>
<td>&gt;50× normal</td>
</tr>
</tbody>
</table>

Exercise

- CK was measured in 32 ultra-distance runners at stages of a 200 km race and 24 hours afterwards

Exercise in muscular dystrophy

Limb girdle, Becker’s, and Fascioscapulohumeral muscular dystrophies

CK was measured before exercise, immediately afterwards, and 24 hours afterwards

Rhabdomyolysis

- Muscle necrosis and release of intracellular contents
- Characterized by muscle pain, weakness, and dark urine, muscle tenderness/swelling
- Clinical concern is risk of renal failure
- Hallmark is elevated CK but no consensus definition based on level of elevation
  - Studies advocate for different thresholds ranging from 5x to 50x the ULN
- Risk of acute kidney injury is low when CK<15,000 U/L on admission
  - Can occur at CK of 5000 U/L
    - Sepsis
    - Dehydration
    - Acidosis

Rhabdomyolysis

- Case series of 26 patients with rhabdomyolysis

Effect of electromyography

- Needle EMG can affect CK level

Cardiac considerations

- Creatine kinase and CK-MB were widely used as biomarkers for myocardial infarction prior to the availability of troponin.
- CK-MB is relatively high in cardiac tissue.
- CK-MB is also increased in skeletal muscle with regeneration of muscle fibers.
  - CK-MB can be increased in patients with chronic muscle disease or in athletes.
Non-neuromuscular Causes of Elevated CK

- Strenuous exercise
- Trauma/Procedures (EMG, injection, surgery)
- Toxins (alcohol, heroin, cocaine)
- Endocrine (hypothyroid, hyperthyroid, hyperparathyroid)
- Electrolyte derangements (hyponatremia, hypokalemia, hypophosphatemia)
- Renal failure
- Viral illness
- Chronic cardiac disease
- Malignancy
- Obstructive sleep apnea
- Neuroacanthocytosis syndromes
- Macro-CK
- Malignant hyperthermia syndromes

Medication Causes of Elevated CK

- Medications
  - Statins
  - Fibrates
  - Colchicine
  - Antipsychotics
  - Zidovudine
  - Certain beta blockers (pindolol, carteolol)
  - Isoretinoin

Effect of denervation on CK

- Creatine kinase can be mildly elevated in conditions causing acute denervation of the muscle
  - Motor neuron disease
  - Motor neuropathies
  - Radiculopathy
  - Plexopathy
Motor neuron disease

- CK levels in patients with ALS (36) and SBMA (33)

| Table 1. Serum CK levels (normal range 52-336 U/L). |
|---------------------------------|----------------|----------------|
|                                 | ALS            | SBMA           |
| Mean ± SD*                     | 304 ± 392      | 939 ± 590      |
| Range                          | 38-2123        | 215-2795       |
| Number of patients with elevated CK level† | 9 of 36       | 28 of 33       |
| Number of patients with CK >1000 U/L | 2              | 12             |

*P < 0.001; †P = 0.005.

Biomarker for muscle disease
Biomarkers

- Objective measures used as a markers of a disease process
- Ideally, only abnormal in the pathological state
- In practice, most biomarkers have variable sensitivity and specificity
Creatine Kinase as a Biomarker

**Pros**
- High in muscle and relatively low in other tissues
- Mostly localized to muscle (95%) and brain
- Measurable in serum
- Enzyme activity is easily measured

**Cons**
- Non-neuromuscular causes of elevation
- Can be elevated in the absence of disease
- Not elevated in all myopathies
Patient with elevated CK

- How do you decide when to pursue further workup?
  - Asymptomatic patient vs patient with weakness
  - What is the likelihood of finding a specific diagnosis?
  - Should we pursue invasive testing (muscle biopsy)?
  - How likely are we to find a treatable cause?
Approach to the weak patient with elevated CK
Signs of possible myopathy

- Proximal weakness
- Atrophy or hypertrophy
- Exercise intolerance
- Family history
- Pigmenturia
- Myotonia
Signs of other neuromuscular disease

- Fatiguable weakness
- Sensory symptoms
- Fasciculations
- Reflex abnormalities
Role of EMG

- Rule out non-myopathic causes of elevated CK
  - Motor neuron disease
  - Motor neuropathy
  - Radiculopathy
  - NMJ disorders
- Determine if there is myotonia (myotonic dystrophy)
- Determine if there are myopathic changes
  - If absent, does not rule out myopathy
Role of muscle biopsy

- Gold standard for the diagnosis of myopathies
  - Histological stains (H&E, Gomori trichrome, Oil Red O, PAS, SDH, NADH, cytochrome oxidase, myophosphorylase, acid phosphatase)
  - Immunohistochemical stains
  - Mitochondrial enzyme activity
  - Glycolytic enzyme activity
  - Electron microscopy
- Biopsy an affected muscle not tested by EMG needle
- Choosing site of biopsy can be assisted with MRI imaging
Yield of muscle biopsy

- Series of 698 muscle biopsies at a neuromuscular referral center
  - Inflammatory myopathy found in 23% of all biopsies
  - Diagnostic biopsy most associated with the group with CK elevated, proximal weakness, and myopathic EMG (specific diagnosis in >50%)

<table>
<thead>
<tr>
<th>EMG and strength status</th>
<th>Probability* of myopathy (%)</th>
<th>Probability* of specific myopathy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Weakness, - EMG</td>
<td>34.3–50.2</td>
<td>7.3–14.6</td>
</tr>
<tr>
<td>+ Weakness, - EMG</td>
<td>39.4–64.2</td>
<td>18.8–27.3</td>
</tr>
<tr>
<td>- Weakness, + EMG</td>
<td>47.6–60.6</td>
<td>25.5–30.7</td>
</tr>
<tr>
<td>+ Weakness, + EMG</td>
<td>74.6–&gt;90</td>
<td>49.9–76.9</td>
</tr>
</tbody>
</table>

*The probability for both myopathy and specific myopathy increased in each scenario in direct proportion to the CK level.

Approach to the patient without weakness with elevated CK
EFNS guidelines on the diagnostic approach to pauci- or asymptomatic hyperCKemia

T. Kyriakidesa, C. Angelinib, J. Schaeferc, S. Saccond, G. Sicilianoe, J. J. Vílchezf and D. Hilton-Jonesg

aClinical Neurosciences, The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus; bDepartment of Neurosciences, University of Padova, Padova, Italy; cDepartment of Neurology, Unterklinikum C.G.Carus, University of Dresden, Dresden, Germany; dCentre de référence des maladies Neuromusculaires, CNRS UMR6543, Nice University Hospital, Nice, France; eDepartment of Neuroscience, Section of Neurology, University of Pisa, Pisa, Italy; fServicio de Neurología, Hospital Universitari La Fe, Valencia, Spain; and gDepartment of Neurology, John Radcliffe Hospital, Oxford, UK

- HyperCKemia defined as CK>1.5 upper limit of normal

<table>
<thead>
<tr>
<th></th>
<th>1.5x ULN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-black male</td>
<td>504</td>
</tr>
<tr>
<td>Non-black female</td>
<td>325</td>
</tr>
<tr>
<td>Black male</td>
<td>1201</td>
</tr>
<tr>
<td>Black female</td>
<td>621</td>
</tr>
</tbody>
</table>

Asymptomatic hyperCKemia

- Asymptomatic
- Pauci-symptomatic
  - No objective weakness on exam
  - No atrophy, hypertrophy, or myotonia
  - Vague neuromuscular symptoms
    - Myalgia
    - Fatigue
    - Exercise intolerance
    - Cramps/stiffness

EFNS guidelines

- Consider and rule out non-neuromuscular causes if appropriate
  - Review medications
  - Substance abuse history (consider tox screen)
  - Check metabolic panel, phosphate
  - Check thyroid function, parathyroid function
  - Consider checking troponin

EFNS guidelines

- Determine family history of neuromuscular disease, hyperCKemia, or malignant hypertension
- Confirm hyperCKemia
  - At least two CK measurements
  - Avoid strenuous exercise for 7 days prior with samples at least 1 month apart
- If hyperCKemia confirmed, check EMG/NCS

EFNS guidelines

- Muscle biopsy recommended if:
  - Myopathic EMG
  - CK >3x normal
  - Patient < 25 years old
  - Exercise induced pain or exercise intolerance
  - Women with CK< 3x normal
    - Can first test blood lymphocytes for Becker/Duchenne mutation

Asymptomatic hyperCKemia

- Multiple case series of muscle biopsy patients with asymptomatic hyperCKemia
- 460 patients from 8 separate studies
  - 134 (29%) were normal
  - 25 (5%) were neuropathic
  - 190 (41%) were nonspecific myopathic
  - 121 (26%) resulted in specific diagnosis
    - 42% metabolic myopathy
    - 21% subclinical muscular dystrophies

Prognosis of asymptomatic hyperCKemia

- D’adda et al reported a 6 year follow up study of 55 patients with asymptomatic hyperCKemia
  - Most remained asymptomatic
  - 1 became symptomatic
  - 45 (78%) still had elevated CK but at a lower level
  - 12 (22%) had normalized CK
  - 1 patient was diagnosed with limb girdle muscular dystrophy
  - 1 patient was diagnosed as a dystrophinopathy carrier

Exercise in asymptomatic hyperCKemia

11 patients with asymptomatic hyperCKemia after maximal and submaximal exercise

Summary
Practical approach

Elevated CK → CK still elevated
- Repeat, avoiding exercise at least 7 days
- Rule out non-muscular and Medication causes

Weak
- EMG
  - Myopathic or nondiagnostic
- Muscle Biopsy
- Not Myopathy

Not Weak→ EFNS guidelines
- Neurogenic process Positive rep stim
Summary

- Creatine kinase is a biomarker with good muscle specificity
- “Normal” values can vary depending on race and sex
- Several factors can elevate CK level in the absence of underlying neuromuscular disease
- Elevated levels in an asymptomatic patient often carry a benign prognosis
- Depending on context, chances of obtaining a diagnostic muscle biopsy can range widely from 7 to 70%.
Thank you!