

**Exercise management & treatment:
How much is too much?
What supplements to take?
Monitoring for rhabdomyolysis**

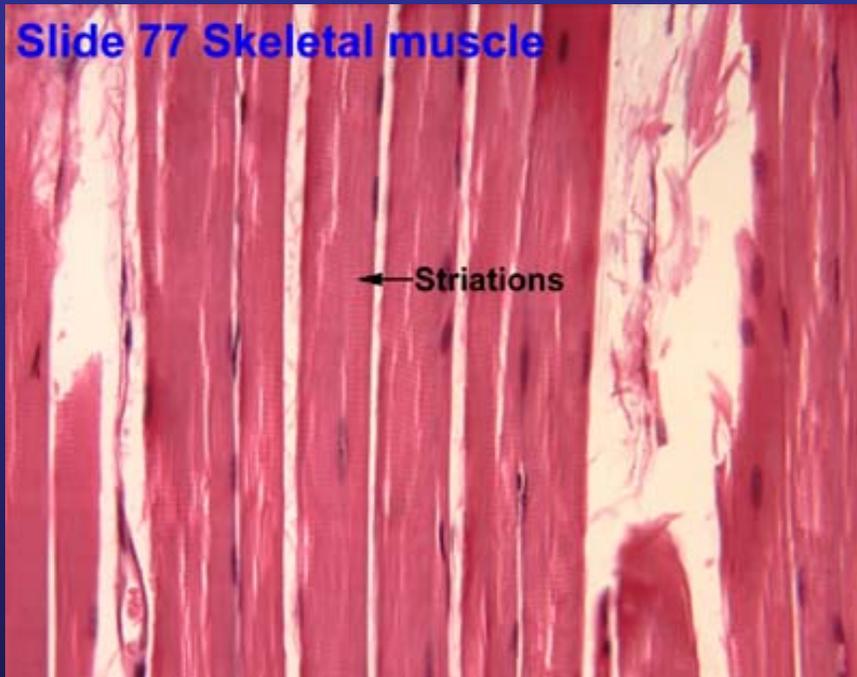
Melanie B. Gillingham, PhD, RD





FAO during exercise

Slide 77 Skeletal muscle

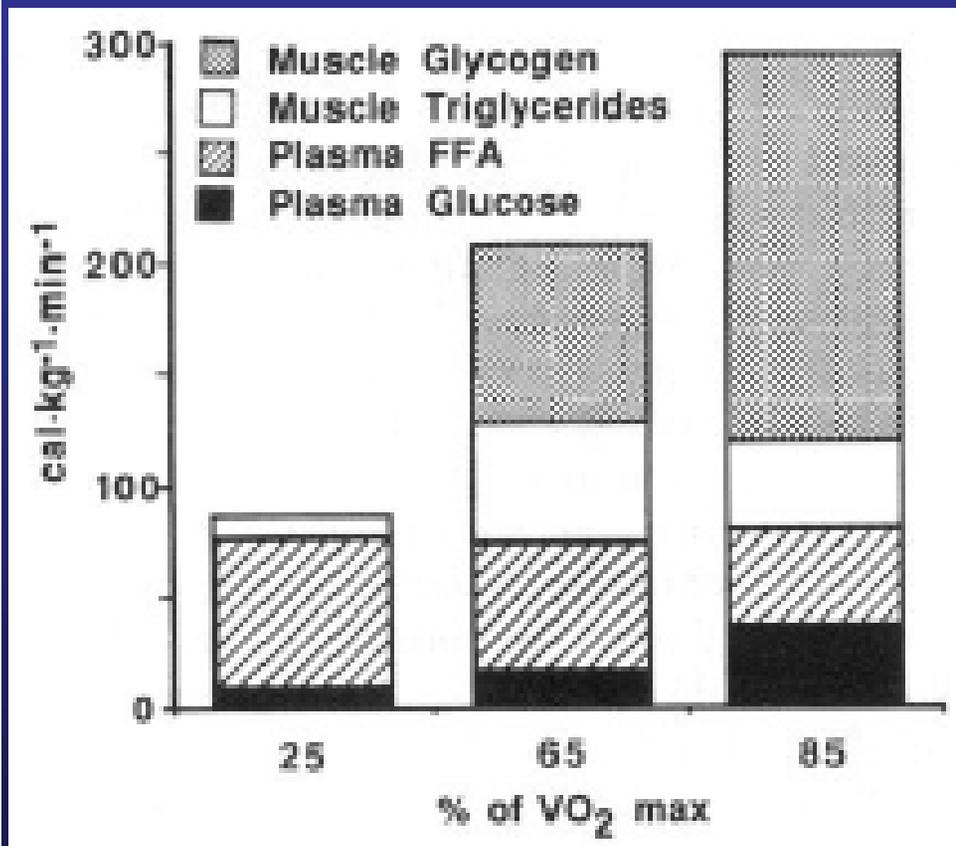


- Skeletal muscle prefers to burn fat for energy
- Cardiac muscle is especially dependent on energy from FAO
- Amount of fat burned during exercise depends on the intensity of the exercise

Muscle Fuels

- Muscle ATP
 - Muscle Creatine phosphate
 - Muscle glycogen
 - Muscle triglycerides
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- Blood glucose
 - Plasma free fatty acids

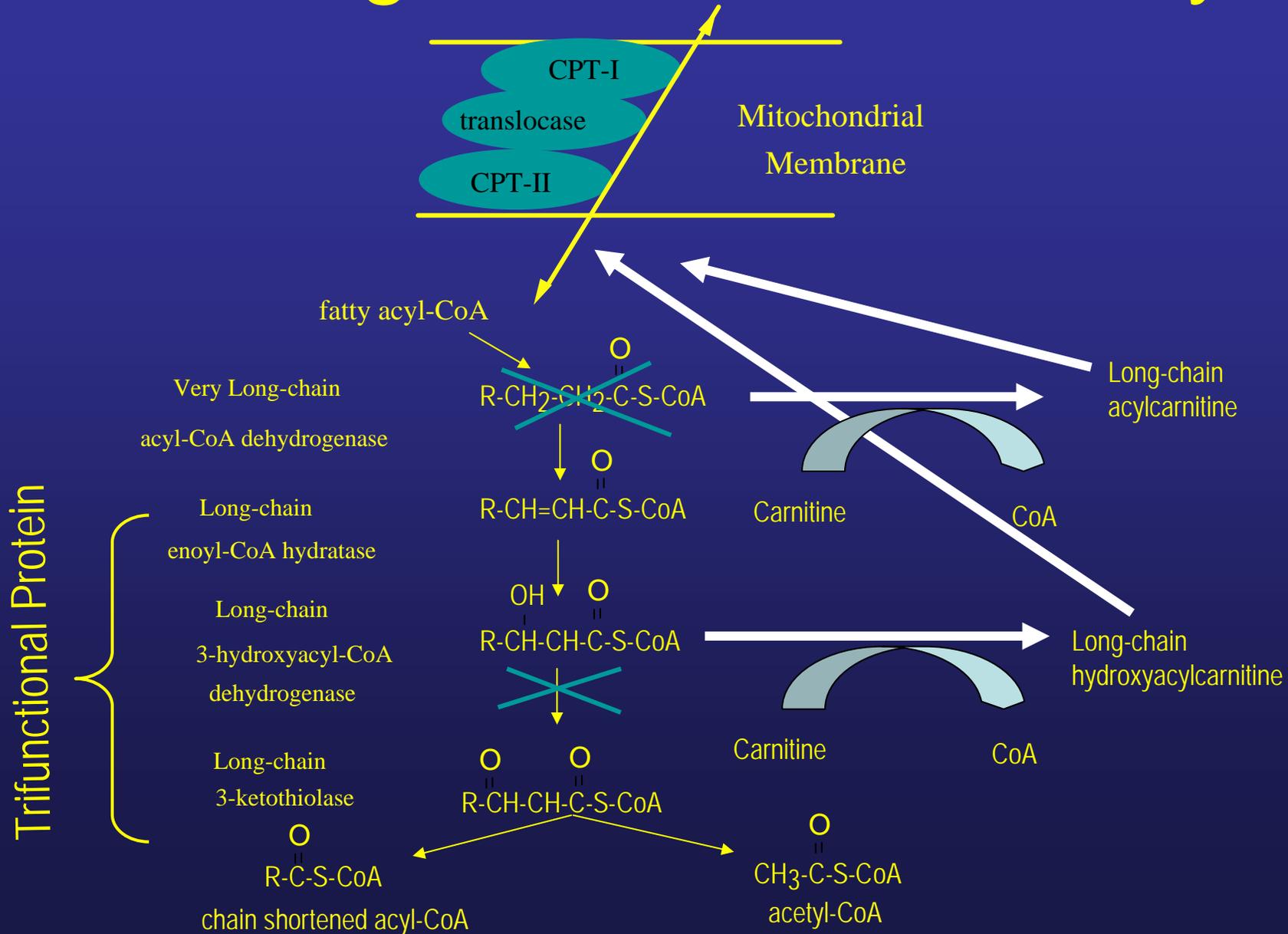
Exercise Intensity & FAO



- Fatty acids can provide 50% or more of muscle energy during low or moderate exercise.

Romijn et al AJP 265:E380-391,
1993

Long-chain FAO Pathway



Rhabdomyolysis & FAO disorders

- Rhabdomyolysis can be a common complication associated with bouts of exercise in FAO disorders
- The exact cause of rhabdomyolysis is unknown.
 - Lack of energy?
 - Toxic effects of metabolites?
- Could supplements prior to exercise prevent rhabdomyolysis?

Exercise Supplements

- MCT for long-chain disorders
- Glucose & fluids
- Coenzyme Q10
- Antioxidants for oxidative stress

MCT supplementation

- Patients with long-chain FAO disorders typically consume MCT supplement at breakfast and/or bedtime but not before periods of activity
- MCT consumed at breakfast may not be available later for oxidation because MCT is preferentially oxidized and not stored as MCT.

Hypothesis

MCT immediately prior to a bout of moderate intensity exercise will provide an alternate fuel for exercise and improve exercise tolerance in children with LCHAD deficiency.

Methods



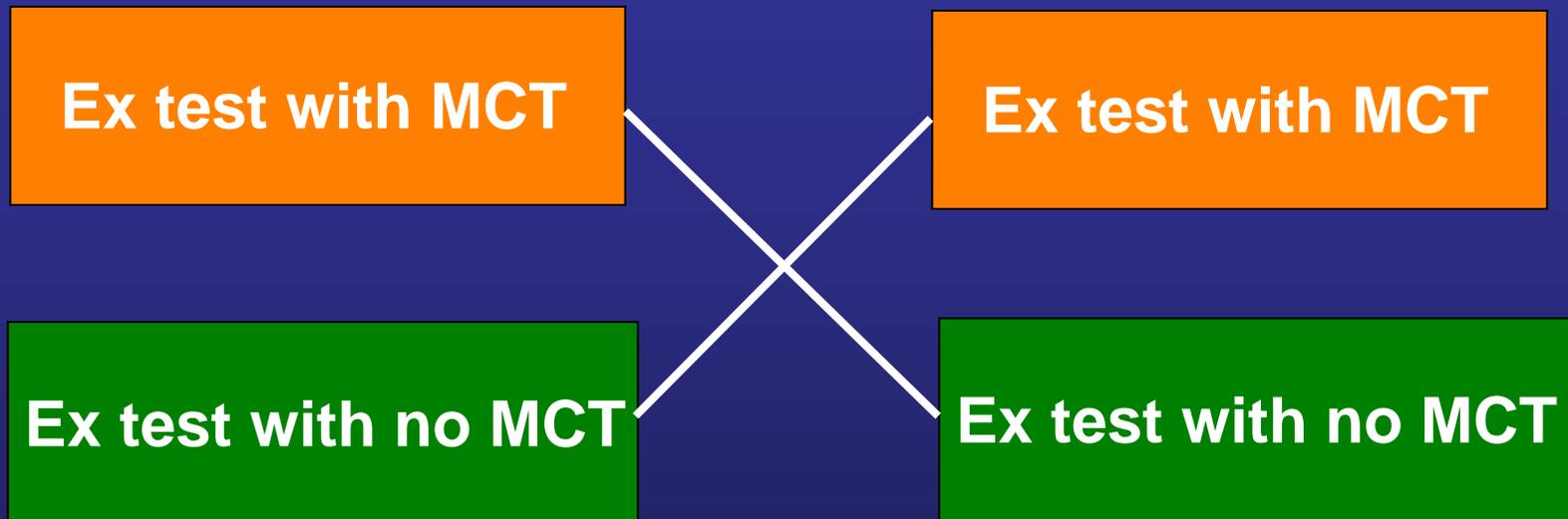
Measured exercise gas exchange HR and blood pressure.

- 20 min prior to exercise drank 4 oz orange juice alone or 4 oz juice + 0.5gm MCT/kg lean body mass
- Immediately prior to exercise, drew pre-exercise blood sample
- 4 min warm-up followed by 40 min exercise at 65-75% estimated max heart rate
- Blood sample taken immediately following exercise (post) and after 20 minutes of rest (recovery)
- Blood analyzed for lactate, CK, ketones and acylcarnitines

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Randomized Crossover Exercise Trial



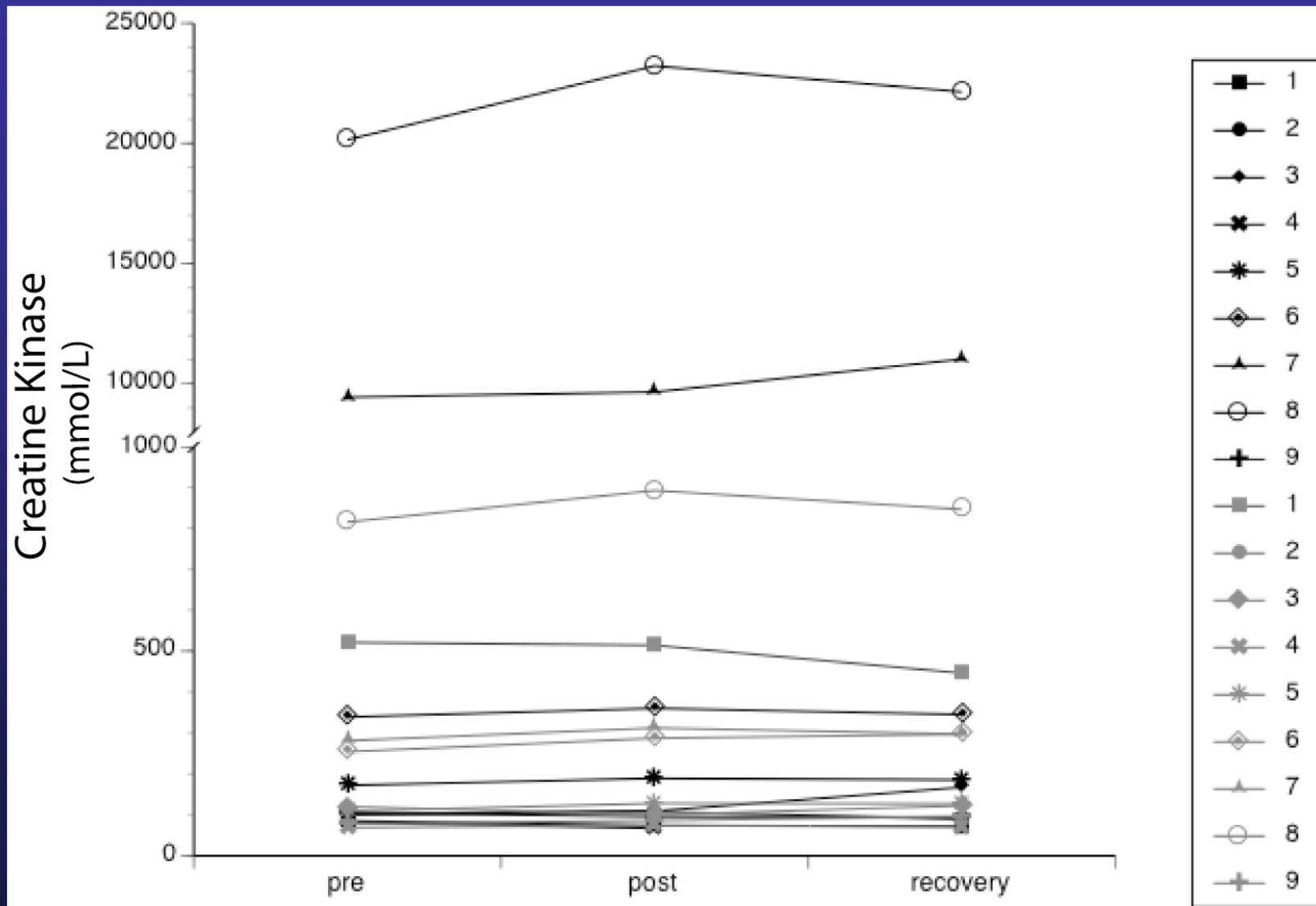
Repeated same grade and speed for the 2nd test

Respiratory Quotient

- No difference in respiratory quotient, RQ
- $RQ \geq 0.95$ primarily carbohydrate oxidation
- Plasma lactate normal in all subjects

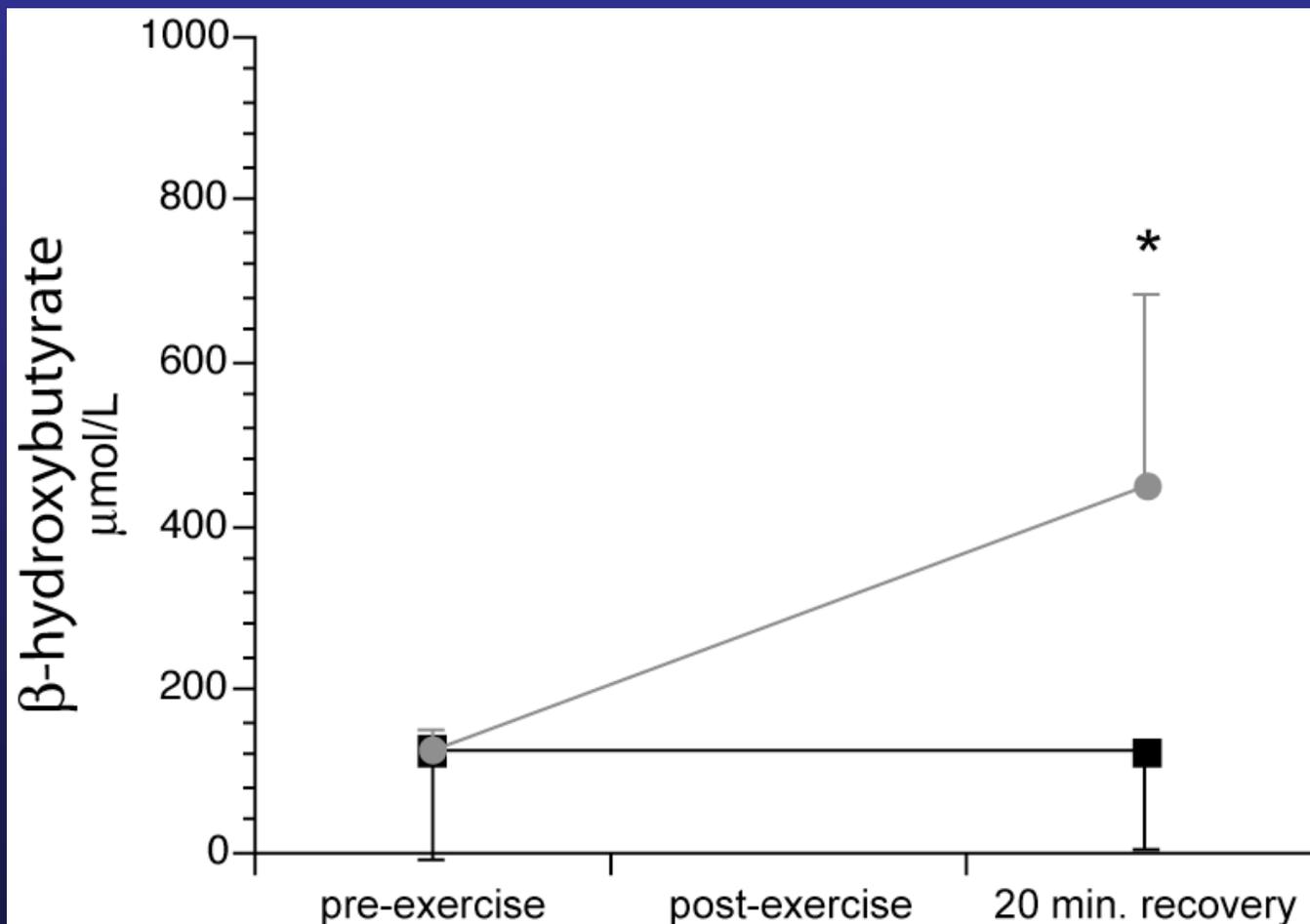
Sub	MCT	No MCT
	RQ	
1	1.05	0.87
2	0.97	0.86
3	1.06	1.01
4	1.01	1.05
5	0.99	1.07
6	0.93	1.01
7	0.89	0.94
8	0.93	0.99
Mean:	0.95	1.01

Exercise did not increase CK



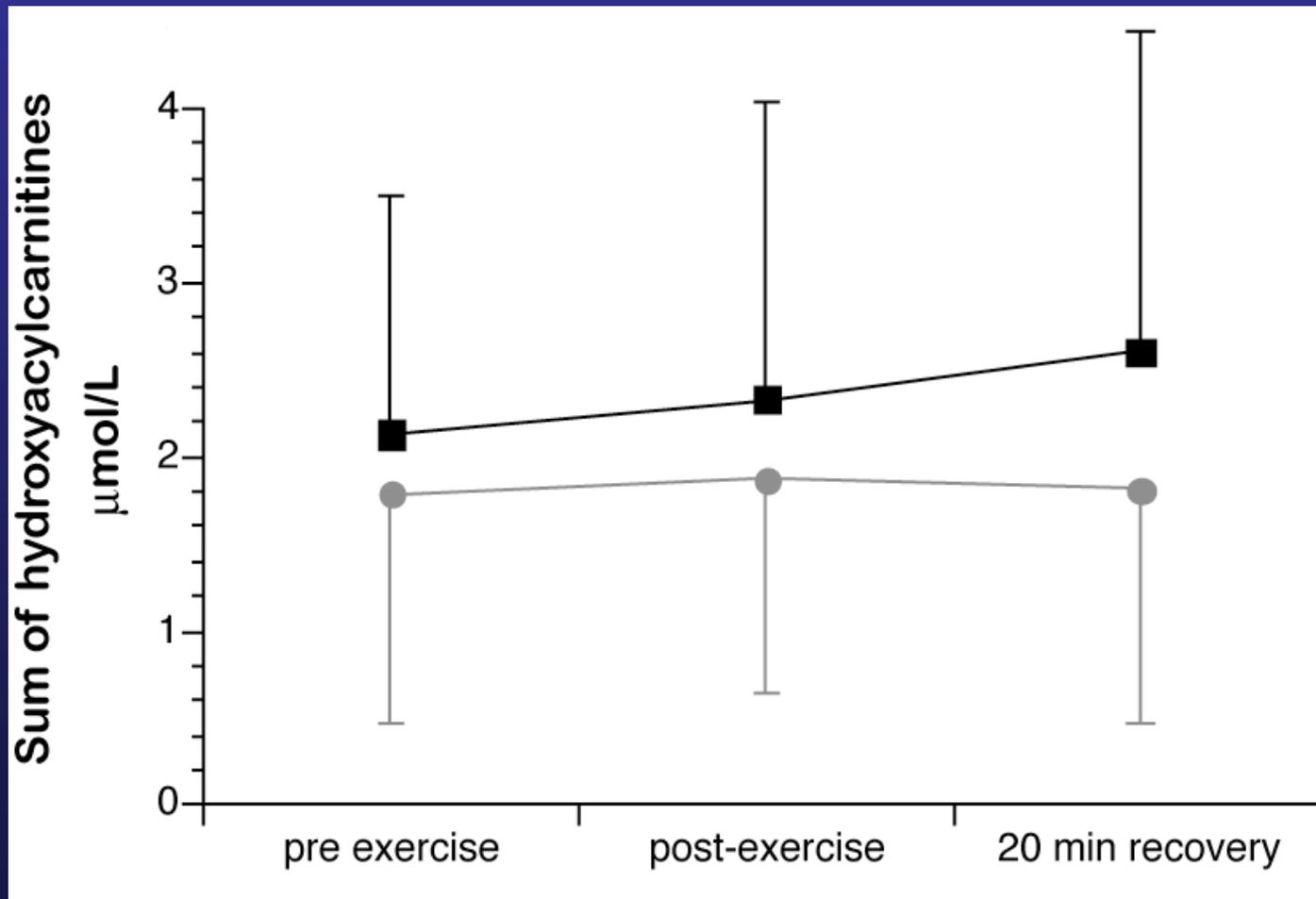
Ketones

Significant increase in ketones with MCT suggesting MCT oxidized during exercise

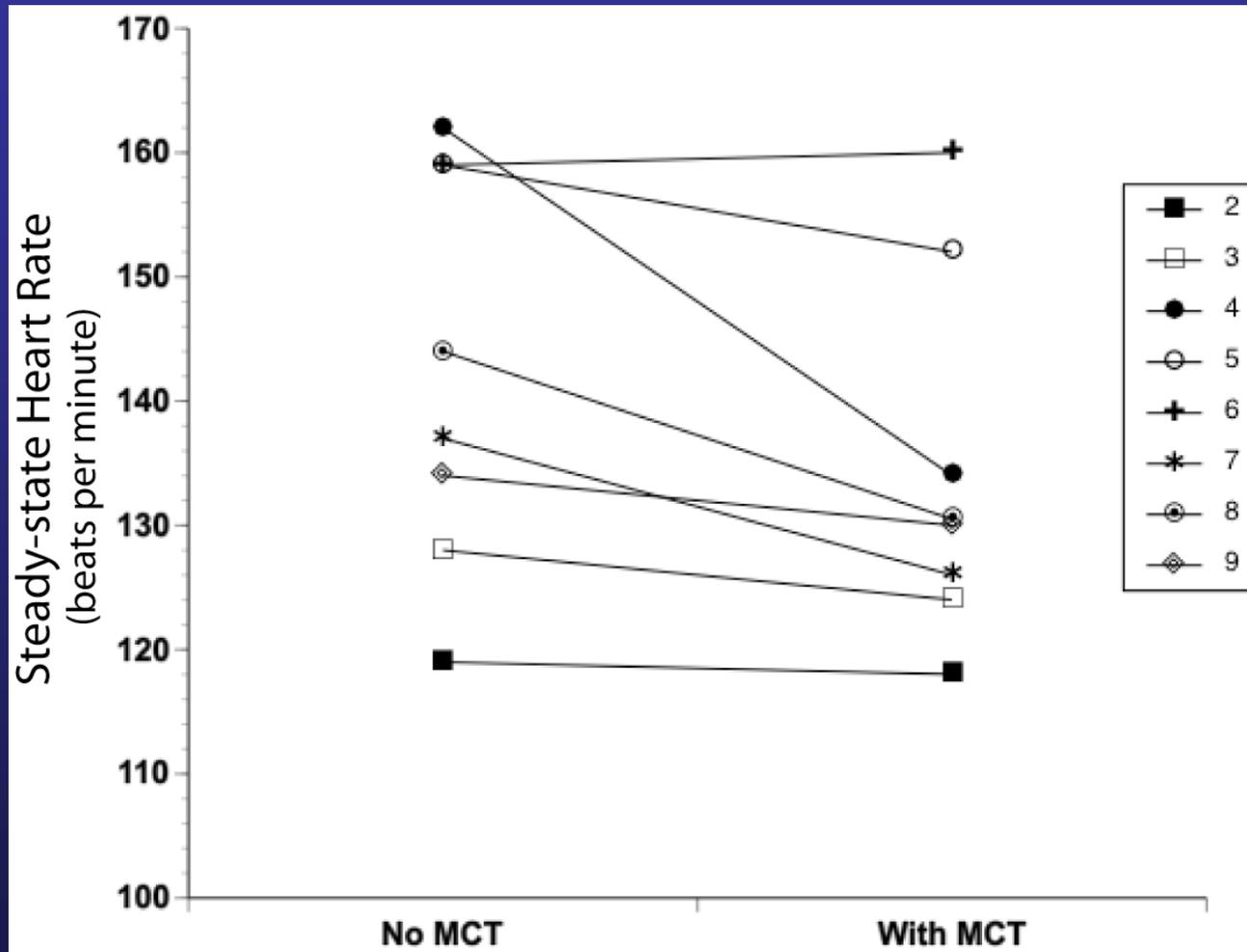


Hydroxyacylcarnitines

Significant ↓ in hydroxyacylcarnitines with MCT



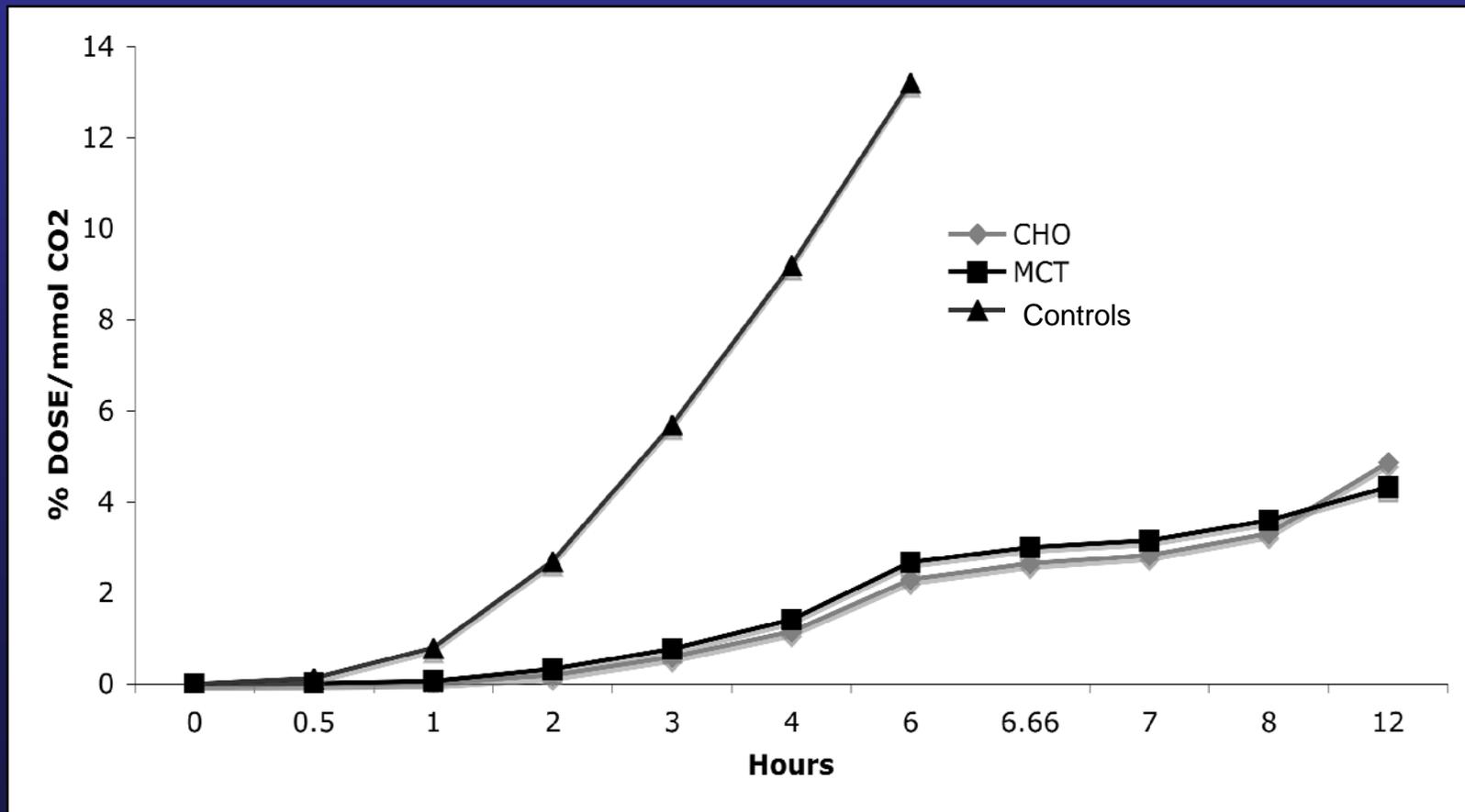
Heart Rate



-significantly lower HR for same work with MCT

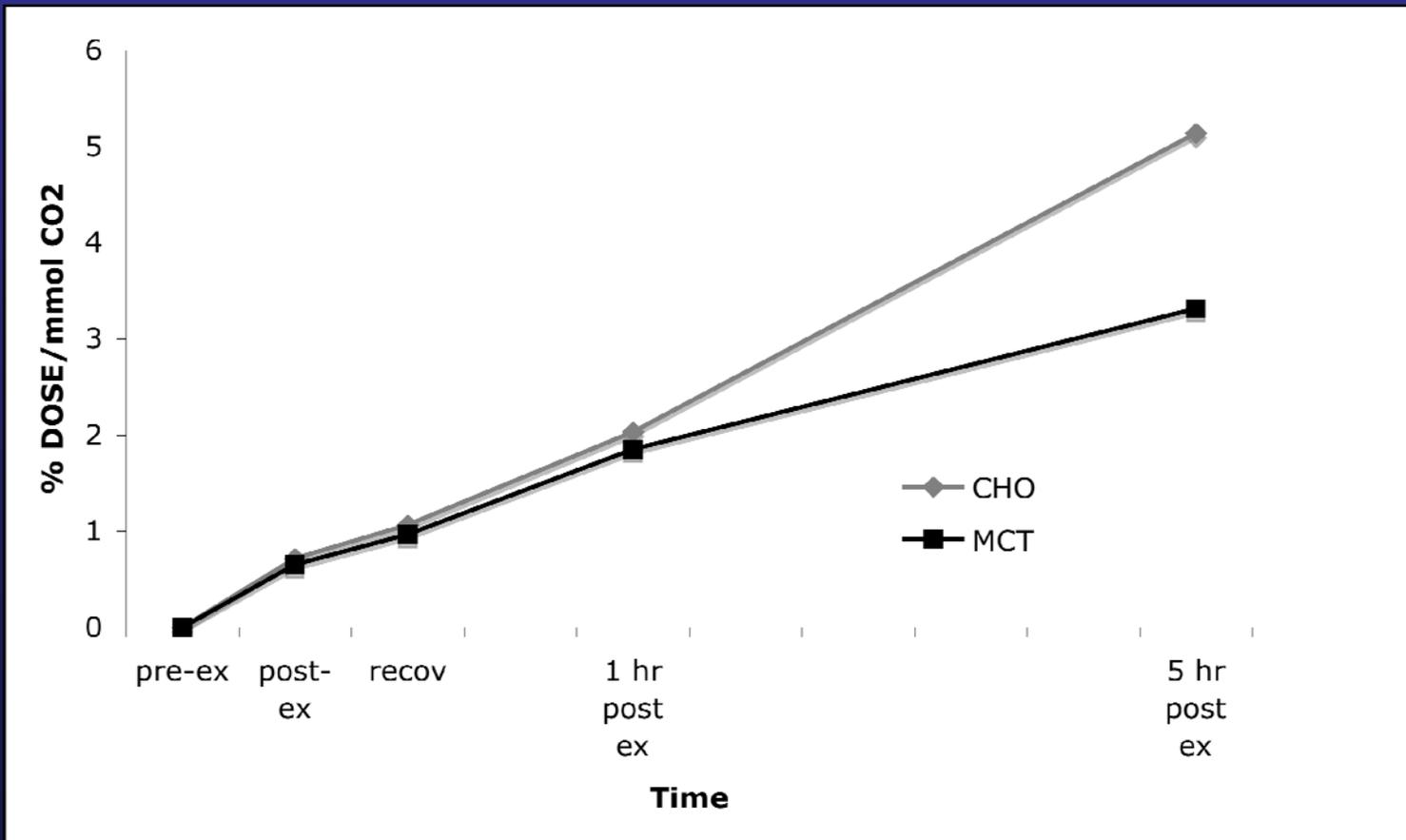
Fatty Acid Oxidation

Patients with LCHAD deficiency oxidized 20% of fatty acids compared to controls.



MCT suppresses Long-chain FAO

MCT prior to exercise lowered post exercise long-chain FAO



Conclusions

- ↑ ketones suggests MCT was used for energy during exercise
- ↓ post-exercise OH-acylcarnitines & ↓ in oleic acid oxidation suggests ↓ in LCFA oxidation
- Plasma CK levels immediately post exercise did not correlate with OH-acylcarnitines or muscle pain
- ↓ Heart rate for same work suggests improved cardiac function

How to get MCT prior to exercise?

- Bake in products such as MCT brownies
- MCT –procal sachet mixed in gatorade

What about glucose?

- Glucose depleted quickly with limited energy supplied from FAO
- Fluids and carbohydrates replenishes muscle energy stores
- IN practice, MCT with a carbohydrate and fluids best prevention of rhabdomyolysis

Other Supplements?

- Coenzyme Q10 thought to improve exercise tolerance in patients with heart failure
 - ½ studies show mild benefit; ½ no change
 - Studies used low # of patients; no studies in children with FAO disorders
- Antioxidants advocated for athletes
 - Vitamin E is a fat-soluble vitamin & antioxidant
 - Subjects with LCHAD deficiency have low plasma vitamin E

How long to exercise?

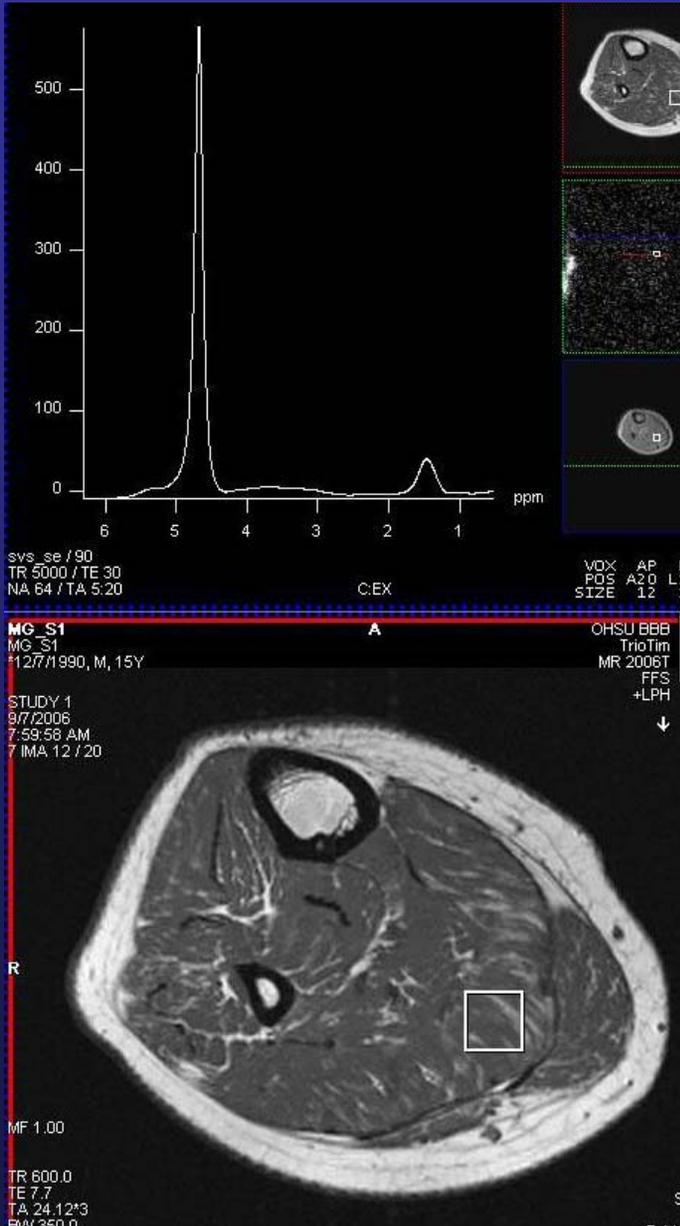
- Moderate intensity exercise for 1 hour appears safe
 - Consume fluids, carbs &/or MCT before and after exercise
 - Don't exercise during or immediately after illness
 - Use extra caution with more frequent breaks in high altitude or high heat

Monitoring for rhabdomyolysis

- Creatine kinase or CK best marker for potential development of rhabdomyolysis
- When should you measure CK?
 - Immediately after exercise not necessarily correlated with metabolites or muscle pain
 - Following morning appears to be most informative

On-going Studies

- Currently recruiting subjects ≥ 8 yrs with TFP, LCHAD & VLCAD def.
- If interested, contact Melanie Gillingham at gillingm@ohsu.edu or (503) 494-1682



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