The Role and Impact of Exercise in Managing Triglycerides and Triglyceride-rich Lipoproteins

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25-minute AGENDA

Overview

Recent trial trends in 2014

Key points in exercise TG metabolism

Principle mechanisms for exercise generated TG reduction

Postprandial TG and remnant lipoprotein response to acute exercise

Provider recommendations
Effects of physical exercise on health-related quality of life and blood lipids in perimenopausal women: a randomized placebo-controlled trial.
N=157 women (40-55 yrs), kuperman index >15. 12 weeks
↓ 9% TG vs controls

Tai chi for primary prevention of cardiovascular disease.
Hartley L. et.al. Cochrane Database Syst 2014; Apr 9;4
Review of 13 trials (1520 participants randomised) and three ongoing trials
↓ 32-40 mg/dL TG reduction

Effect of Exercise Intervention on Changes in Free Fatty Acid Levels and Metabolic Risk Factors in Stroke Patients
N=20 male stroke patients 47-59 yrs; 5X/wk, 12 weeks
↓ 22% TG

Effects of high-intensity circuit training, low-intensity circuit training and endurance training on blood pressure and lipoproteins in middle-aged overweight men
Paoli et.al. Lipids in Health and Disease 2013, 12:131 Padova Italy
N=58 men, 61 yrs, BMI 29.8 randomly assigned to one of the 3 exercise treatment groups: HICT, LICT and ET. Rx 3X/wk, 50 min per session for 12 weeks.
↓ 15% TG

Effects of Moderate- and Intermittent Low intensity Exercise on Postprandial Lipemia.
N=9 men MOD and LOW reduced incremental TG area under the curve 34 and 20% respect.
A randomised trial comparing weight loss with aerobic exercise in overweight individuals with coronary artery disease: The CUT-IT trial.


↓ 25% TG after 12 weeks of cycle AIT @ 90% MV02 (P=.03)

Effects of Regular Physical Exercises in the Water on the Metabolic Profile of Women with Abdominal Obesity.

Kasprzak Z, et.al. J Hum Kinet. 2014 Jul 8;41:71-79
32 women aged 41-72 years 3 months Ex

11% reduction in TG

Impact of exercise training without caloric restriction on inflammation, insulin resistance and visceral fat mass in obese adolescents.

Bottom line

So how much TG reduction can we expect from a 12-16 week aerobic exercise program of sufficient energy expenditure:

✓ Exercise programs have been shown to decrease fasting TGs by 4–37% (approximate mean change of 24% depending on baseline fasting TG).

Fletcher, 2005
Helge, 2006
Trejo-Gutierrez, 2007
Kraus, 2009
Magkos, 2010
Variables influencing TG response to exercise and exercise training

Baseline TG
Session energy expenditure
Exercise intensity
Apo C and E genotypes
Fatty acid transporters
VLDL clearance
Muscle TAG stores
Hepatic and lipoprotein lipase
Post-prandial influences
Gender *

* Women use more intra-muscular TAG as energy source during moderate-intensity exercise than men, possibly because they have higher baseline (i.e., resting) intra-muscular TAG content
Key Point 1

The **acute** TG response to a single session of exercise, e.g., 400 kcal 4-mile walk

vs

**Chronic** TG response to exercise training, e.g., 2000 kcal/wk,

= contrasting TG responses
What is the most immediately available form of TG for oxidative energy production in contracting muscle?

a. Plasma free fatty acids (albumin-bound)
b. Plasma VLDL - TG
c. Intramuscular TG
d. Adipose tissue TG
Key Point 2

The source of exercise generated fatty acid oxidation in muscle:

- Plasma fatty acids
- TG carried/stored in Very low density lipoprotein particles
- TG stored in muscle – IMTG - then hydrolyzed to free fatty acids for mitochondrial uptake and oxidation
- Adipose tissue
Intramuscular TG Storage

IMCL, intramyocellular lipid
Interaction of Exercise Duration and Exercise Intensity and Fatty Acid Oxidation

i.e., exercise time and speed

A counterintuitive assumption/misconception
During prolonged exercise there is a shift from CHO metabolism toward fat metabolism.

The rate of FFA oxidation is relatively low at long-durations.
Exercise Intensity and Fuel Selection

Powers & Howley 2009

Yes, lots of proportional FA usage but the rate of FA oxidation is very low

55-60% optimal intensity for prolonged EE
Restriction of physical activity (e.g., sedentary or sitting time) has been reported to result in a 10-fold decrease in lipoprotein lipase activity in red oxidative muscle fibers and in adipose tissue. This transiently increases TG and decreases HDL-C.

Bey 2003
Hamilton 2003
Katamarzyk & Church 2009
Exercise-induced TAG-lowering is acute, in that it manifests after just a single bout of exercise and is not the result of repeated exercise sessions (i.e., training), and short-lived, as it is readily reversed when exercise is withdrawn (i.e., detraining).

Numerous studies have confirmed this initial hypothesis: the magnitude of the decrease in plasma TAG concentration after a single exercise session and after training is the same (i.e., 15–50%).

These observations suggest that chronic exercise does not have an equally sustainable effect on plasma TAG concentration, i.e., beyond that attributed to acute exercise; hence exercise should be performed on a regular and uninterrupted basis to maintain hypoTG.
• An apparent energy expenditure threshold, more exercise does not seem to result in greater decreases in fasting plasma TAG concentrations although it may produce a somewhat longer-lived effect.

Annuzzi 1997
Zhang 2007
Ferguson 1998
• The magnitude of TAG-lowering in response to a single bout of exercise of the same duration and relative intensity is similar in obese and lean subjects, and men and women but greater in trained than untrained subjects.

Gill 2004, 2002
• 400-500 kcal of aerobic exercise performed 12–16 h prior to a meal seems to produce the most dramatic and consistent decrease in postprandial lipemia (TG and TGRL’s)

*400-500 kcal = ~ 4-5 mile run or 6-8 mile walk

Peddie 2012
Maraki 2010
Burns 2005
Shannon 2005
• Delayed-onset hypotriacylglycerolemia in the basal state, 1 day after a single bout of endurance exercise is due to augmented efficiency VLDL-TAG removal from the circulation, likely mediated by the secretion of fewer but TAG-richer VLDL particles from the liver;

Exercise-induced changes in skeletal muscle lipoprotein lipase are more likely a contributing rather than the primary factor of TAG-lowering.
• The exercise-induced increase in basal VLDL-TAG clearance rate plateaus at 40%, whereas the threshold of energy that needs to be expended during endurance exercise lies near or above 500–600 kcal.

Resistance exercise is more potent than endurance exercise in this respect.

Magkos 2009
• The type of endurance exercise, i.e., cycling or running, does not appear to affect the VLDL-TAG metabolism response to exercise, despite differences in muscle recruitment and substrate oxidation rates during these two types of activity.

Magkos 2006
Tsekouras 2007
Achten 2003
Exercise and Postprandial Lipemia/TG

Response to fatty meals
Fat load (12 - 22 grams) and/or glycemic load + Caffeine load (40-200 milligrams)
Quantitative Review of Exercise and PPTG

38 effects from 555 subjects, 28 studies

\[ r = 0.62 \]

Prior exercise EE kcal (kcal)

Petitt D & Cureton K  Metabolism. 2003;4:418
Preprandial Exercise and Postprandial Lipemia

Hours after high fat meal

TG mg/dL

0 2 4 6 8

Preprandial Exercise and Postprandial Lipemia

400-500 kcal ex of prior exercise

Maraki 2013
Trombold 2013
Hashimoto 2013
Gabriel 2013
Ho 2011
Mestek 2011
Farah 2010
Magkos 2009
Smith 2004
Petitt 2003
Thomas 2000
Zhang 1998
Postprandial Lipemia (TG) Issues

- TG time/area under the curve is greater with T2D, visceral ob, & MetSyn
- Decreased arterial endothelial function
- Decreased HDL-C response
- Increased chylomicron, & IDL- VLDL remnant exposure

Maraki 2013
Napolitano 2013
Nakajima, 2012
Wojczynski, 2011
Giannattasio, 2005
Wang, 2011
Hajer, 2008
Kris-Etherton, 2007
Nestel, 2001
Whitman, 1998
Zhang, 1998
Exercise plus n-3 fatty acids: Additive effect on postprandial lipemia
Smith BK et. al. Metabolism 2004;53:1365 (Univ. of Kansas)

N = 10 healthy males (25yrs)
Supplementation consisted of 4.0 g of n-3FA per day for 5 weeks.

Results: TG peak ↓ 38% by n-3FA supplementation and 50% by the combination of exercise and n-3FA supplementation.

When compared with the exercise trial, the TG-AUC_T during the combined trial was significantly lower.

Exercise: 40%
n-3FAs: 42%
Ex + n3: 58%
The chronic effects of fish oil with exercise on postprandial lipaemia and chylomicron homeostasis in insulin resistant viscerally obese men


- 29 men with metabolic syndrome were randomly assigned to take fish oil or placebo for four weeks, before undertaking an additional 12 week walking program.

- Supervised walking sessions, 3-5 X week @ 474 kcal per session

- 4 fish oil capsules (providing a total of 1000 mg EPA and 700 mg DHA) or four placebo tabs/day with meals. 1.7g n3

Results: Combining fish oil and exercise resulted in a significant further reduction in the fasting apo B48 concentration, concomitant with attenuation of fasting TAG concentrations and the postprandial TAGIAUC response - ↓ 22%.

✓ An effective therapeutic strategy for the chylomicronemia in subjects with MetS is the combination of chronic, regular exercise and a relatively low dose of fish oil.
The chronic effects of fish oil with exercise on postprandial lipaemia and chylomicron homeostasis in insulin resistant viscerally obese men
We therefore conclude that an effective therapeutic strategy for the chylomicronemia in subjects with MetS is the combination of chronic, regular exercise and a relatively low dose (~2g) of fish oil.

Karin Clark  *Nutrition & Metabolism*  2012, 9:9
Overall Characteristics of Exercise Quantity Required to Reduce Postprandial Lipemia

- **Total exercise energy expenditure volume** (kcal) in a single session appears to be more important than exercise intensity.
- Ideal acute exercise volume is: \( \geq 50 \text{ min or } \geq 400 \text{ kcal} \) (minimum 45 minutes).
- Continuous or interval exercise of equal total kcal have similar TG-AUC effects (e.g., 10 4-min bouts vs 1 40-min bout).
- Ideal timing of exercise prior to fatty/glycemic meal is 8-12 hrs (6-24 hr range).
- The magnitude of postprandial TG reduction ranges from 25-50%.
- The TG reduction is relatively short-lived (24-36 hrs).
- \( \uparrow \) PPTG response is greatest when \( \geq 50 \text{g of fat} \) are consumed although several studies demonstrated response at lower intake values.
Summary

• Exercise training programs (eg. 3-4 months of aerobic activity 5-7 days a week) appear to reduce plasma TG 4-37%

• Single exercise session TG reductions range from 15-50%

• The acute TG response to a 400 kcal dose of exercise appears to be limited to 24-36 hours

• Postprandial TG and TGRL response to high fat (and high glycemic) meals is attenuated by the volume and timing of prior exercise (8-12 hours earlier, ~400 kcal PA)