

# Exercise to Lower Postprandial Lipemia: Why, When, What and How

## Authors

Anatoli Petridou , Vassilis Mougios

## Affiliation

School of Physical Education and Sport Science at Thessaloniki, Laboratory of Evaluation of Human Biological Performance, Aristotle University of Thessaloniki, Thessaloniki, Greece

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## Correspondence

Dr. Anatoli Petridou

Aristotle University of Thessaloniki, Physical Education and Sport Science, TEFAA, Aristotle University of Thessaloniki 54124 Thessaloniki Greece

Tel.: +302310992237, Fax: +302310995282

apet@phed.auth.gr

## ABSTRACT

We review recent findings on the ability of exercise to lower postprandial lipemia (PPL). Specifically, we answer why exercise is important in lowering PPL, when it is most effective to exercise to achieve this, what the preferred exercise is and how exercise reduces PPL. Most findings confirm the power of exercise to lower PPL, which is an independent risk factor for cardiovascular disease. Exercise is most effective when performed on the day preceding a high- or moderate-fat meal. This effect lasts up to approximately two days; therefore, one should exercise frequently to maintain this benefit. However, the time of exercise relative to a meal is not that important in real-life conditions, since one consumes several meals during the day; thus, an exercise bout will inevitably exert its lowering effect on PPL in one or more of the subsequent meals. Although moderate-intensity continuous exercise, high-intensity intermittent exercise, resistance exercise and accumulation of short bouts of exercise throughout the day are all effective in lowering PPL, submaximal, high-volume interval exercise seems to be superior, provided it is tolerable. Finally, exercise reduces PPL by both lowering the rate of appearance and increasing the clearance of triacylglycerol-rich lipoproteins from the circulation.

## Introduction

Postprandial lipemia (PPL), defined as the rise in circulating triacylglycerols (TAG) following a meal, is an issue of concern to the medical community because it is considered an independent risk factor for cardiovascular disease (CVD) [1]. Two non-pharmaceutical ways to lower PPL are reducing fat intake and increasing exercise/physical activity; the latter has been found to be more effective [2].

Postprandial TAG derive primarily from lipoproteins of intestinal (chylomicrons) and hepatic origin (very low-density lipoproteins, VLDL). Circulating total, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol concentrations are barely influenced by normal food intake or after an oral fat load [3, 4]. PPL is usually measured through repeated blood sampling for 3 to 8 h after a meal and is typically presented as TAG concentrations at the different sampling points, area under the curve (AUC) or incremental AUC (iAUC), the latter being calculated by subtracting the fasting concentration from postprandial concentrations.

The scientific literature concerning the effect of exercise on PPL displays a large variety of study designs regarding (i) exercise type, intensity and duration, (ii) meal content, (iii) timing of exercise relative to the test meal(s) and (iv) characteristics of the participants. This makes it difficult to produce a clear picture of the effect of exercise on PPL. Nevertheless, previous reviews on both healthy and diseased individuals have concluded that exercise has an acute, moderate lowering effect on PPL, with a positive influence of the energy expenditure of endurance exercise [5–13].

The aim of this review is to present an update covering the effect of exercise on PPL. We will discuss *why* exercise is important, *when* it is more effective to exercise relative to a meal, *what* is the preferred exercise and *how* exercise lowers PPL.

## Criteria for study inclusion

The review was mainly based on a PubMed search for studies including one of the terms, “exercise,” “physical activity” and “exer-

cise training,” and one of the terms, “postprandial lipemia,” “postprandial triacylglycerol” and “postprandial triglycerides,” published from 2014 to present (unless our reference to earlier studies served a specific purpose or a reference was not included in previous reviews), as the detailed reviews by Maraki and Sidossis [8] and Freese and coworkers [10] cover the issue up to 2014. Additional studies were found through the reference lists of some studies. To be included in the review, studies had to be on humans, with adequate description of the exercise and test meals used, with at least 3 h of postprandial TAG measurements, with a no-exercise control and written in English.

### Why is exercise important in lowering PPL?

The answer to this question lies in the following:

- i. Most individuals are in a postprandial state during the largest part of the time they are awake, as they usually consume two to three main meals and intermediate snacks during the day. Additionally, dietary patterns characterized by high consumption of fat and carbohydrate, which prevail in many modern societies, lead to high PPL [4, 14].
- ii. PPL plays a crucial role in the formation and development of atherosclerosis, mainly through endothelial dysfunction, oxidative stress and inflammation; this makes PPL an independent risk factor for CVD [1]. Specifically, PPL is connected to atherogenicity through the remnants of postprandial lipoproteins, which infiltrate the arterial wall, leading to the accumulation of atherosclerotic plaques, and through changes in HDL and LDL (decreased HDL cholesterol and increased small-dense LDL particles) [5]. Epidemiological studies have found that an increase of 1 mmol/L (88.5 mg/dL) or higher in non-fasting, or postprandial, circulating TAG concentration is associated with increased risk, ranging from 1.2 to 16.8-fold, of CVD and death [15, 16]. Additionally, an increase of 1 mmol/L (39 mg/dL) in plasma non-fasting remnant cholesterol (a marker of which is postprandial TAG) is associated with a 2.8-fold causal risk for ischemic heart disease [17]. Attesting to the deleterious effects of PPL, a panel of experts [18] and the European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine [19] have recommended the replacement of fasting by non-fasting plasma TAG concentration in the assessment of CVD risk, with a non-fasting concentration of  $\geq 220$  mg/dL ( $\geq 2.50$  mmol/L) indicating increased CVD risk [18]. It has been suggested that individuals with fasting TAG  $< 70$  mg/dL will likely not exceed postprandial TAG of 220 mg/dL and individuals with fasting TAG  $> 130$  mg/dL will likely exceed postprandial TAG of 220 mg/dL, whereas individuals with fasting TAG between 70 and 130 mg/dL should be recommended for postprandial TAG testing [20]. Thus, decreasing postprandial lipid concentrations could be a measure against CVD.
- iii. Exercise lowers PPL, as has been concluded by reviews [8, 10] and will be further shown in the present update, although the clinical relevance of this effect is limited. To document this, we examined how many of the original studies that are included in the present review and showed a significant effect of exercise on PPL satisfied the criterion of lowering circulating TAG by at least 1 mmol/L, which is the minimal established clinically relevant effect [15, 16]. On this basis, 7 studies demonstrated a

clinically relevant effect, with an average TAG reduction of 38% (range 29 to 47%) [21–27], whereas 42 studies did not find a clinically relevant effect, with an average TAG reduction of 22% (range 4 to 35%) [14, 28–68].

- iv. In addition to its postprandial TAG lowering effect, exercise plays an important role in improving inflammation [69], reducing oxidative stress [39], and protecting the vasculature from the deleterious effects of a high-fat meal [70–72], although evidence for a lack of such effects also exists [73–75].

Thus, the short answer to the title question (why is exercise important in lowering PPL?) is: Exercise lowers PPL, which characterizes large parts of the day and is an independent risk factor for CVD.

### When is it most effective to exercise to lower PPL?

To facilitate the examination of this question, we have grouped studies according to the timing of exercise relative to the test meal(s) and according to the fat content of the test meal(s). Moreover, we consider the chronic effect of exercise (that is, training) on PPL.

#### Exercise performed on the day preceding a high-fat meal

Since 2014, 36 studies have confirmed that exercise performed on the evening prior to a morning high-fat meal (that is, a meal containing above 0.7 g of fat per kg body mass) lowers PPL, compared to no exercise. This has been shown in young, middle-aged and/or older men [14, 21–23, 27–43, 76, 77], young men and women [44], young or middle-aged women [45, 67], normal and overweight individuals [68], overweight and obese individuals [24, 46, 47] and adolescent boys and girls [48–53].

On the other side, 13 studies have reported no significant effect on PPL when exercise was performed on the evening preceding a morning high-fat meal. Specifically, this has been shown in men [39, 70, 78–82], older adults [79, 83], postmenopausal women [84], overweight and obese individuals [73, 85] and adolescent boys and girls [86, 87]. It is worth mentioning that there is a great diversity of types of exercise performed in these studies.

A possible explanation for not finding a lowering effect of exercise on PPL is the compensation for the energy expenditure of exercise through a meal [73]. Immediate replenishment of the exercise-induced energy deficit diminished the reduction in PPL [43, 64, 88]. Along the same line, previous studies have shown that maintaining an exercise-induced energy deficit resulted in a greater reduction in TAG iAUC, compared to restoring energy balance through food intake [10], although previous data demonstrated greater reduction of PPL with exercise compared to equivalent dietary energy deficit [89]. A factor that may modulate the role of compensation for the energy expenditure of exercise through a postexercise meal is its carbohydrate content, as a low-carbohydrate meal did not diminish the lowering effect of exercise on PPL, whereas an isoenergetic high-carbohydrate meal did [27]. In overweight and obese individuals, consumption of low-glycemic index carbohydrates after exercise did not diminish the attenuation of PPL, whereas consumption of high-glycemic index carbohydrates did, which was attributed to the suppression of fat oxidation by the higher insulin response to the high-glycemic index meal [24]. Nevertheless, replenishment of the exercise energy expenditure by glucose did not

affect the exercise-induced decrease in PPL, possibly because of an absence of an effect on the insulin response [21].

Habitual physical activity may be a determinant of the effect of acute exercise on PPL, since recent studies have shown that exercise performed on the evening prior to a high-fat meal failed to reduce PPL when daily step count was low (< 5000 steps) and/or sitting time was long, as opposed to high daily step count (8500 steps) [90–92]. This effect has been termed “exercise resistance” [92].

#### Exercise performed on the day preceding a moderate-fat meal

A few studies examining the effect of exercise on PPL have used test meals of moderate fat content (that is, 0.4 to 0.7 g of fat per kg body mass) to be closer to real-life settings. All support a lowering effect of exercise, performed approximately 12 h before the test meal, on PPL compared to no exercise. This has been shown in adults [54, 55], postmenopausal women [56, 57] and adolescent boys [58].

#### Exercise performed on the day of a high- or moderate-fat meal

Many studies have examined the effect of exercise on PPL when exercise is performed on the same day as the test meal. This includes the following cases: (i) exercise before the test meal, (ii) exercise after the test meal and (iii) exercise both before and after the test meal.

Most of the studies that employed exercise immediately to 1 h before a high-fat meal found no effect on PPL in lean and obese men [93, 94], trained men [95, 96], hypercholesterolemic individuals [59, 97] and adolescents [60, 71]. This was also the case with low/moderate-fat meals in obese adults [98, 99] and individuals with chronic paraplegia [100].

In contrast, there are studies that have reported a lowering effect of exercise, performed 30 min to 1 h before a high-fat meal, on PPL in adults [25, 59] and girls [60]. A lowering effect was also found when exercise was performed 2 h before a high-fat meal in overweight and obese men [61] and in postmenopausal women [26], as well as 4.5 h before a high-fat meal in men with prediabetes [62]. Interestingly, a pre-exercise fructose drink (low glycemic index) resulted in lower PPL after a high-fat meal that was administered immediately after exercise, as compared to a pre-exercise glucose drink (high glycemic index) [101].

Another study design, closer to real-life conditions, involves short bouts of exercise that interrupt prolonged sitting (with or without comparison to continuous exercise), performed between two or three meals (breakfast, lunch and dinner) during the day. A variety of exercise types and timing patterns have been used. A recent meta-analysis found that regular activity breaks from prolonged sitting (“exercise snacks”) did not change PPL when compared to prolonged sitting [102]. A subsequent meta-analysis reported a small effect of breaking up sitting with physical activity on attenuating PPL, whereas there was no difference between exercise snacks and a bout of continuous exercise [103]. Both meta-analyses showed that exercise snacks were more effective in lowering PPL when performed the day before the test meal [102, 103].

Results from original studies following (or not included in) the aforementioned meta-analyses are similar. Breaking up prolonged sitting with standing, walking, chair squats, resistance exercise (RE) or stair climbing in young healthy individuals [104–106], individuals with increased cardiometabolic risk [106–110] and older women [109] on the day of the test meals did not affect PPL.

However, there are data supporting reduced PPL by frequent interruptions of prolonged sitting with light- and moderate-intensity walking breaks in young obese men [63] and postmenopausal women [26]. Additionally, accumulating short bouts of brisk walking throughout the day reduced PPL in older women, although dietary replenishment of the exercise-induced energy deficit diminished this effect [64]. Finally, PPL was reduced by a combination of moderate-intensity continuous exercise (MICE) and exercise snacks, relative to uninterrupted sitting, in men and postmenopausal women over 55 y, suggesting an additive effect [65].

#### Exercise performed after a high- or moderate-fat meal

Many people exercise in the postprandial, rather than postabsorptive, state, as modern lifestyles include a large number of meals and snacks during the day. Reviews have concluded that, although post-meal exercise is more beneficial than pre-meal exercise in lowering postprandial hyperglycemia in healthy individuals and individuals with type 2 diabetes [111, 112], pre-meal exercise is superior to post-meal exercise in lowering PPL [111].

In accordance with this conclusion, no difference in PPL was found between walking immediately to 1 h after a high-fat or Mediterranean-diet meal and resting [74, 113, 114]. Curiously, exercise split between the early pre- and postprandial periods resulted in a higher lipemic response, compared to no exercise [94]. On the contrary, RE performed 2 h after a high-fat meal attenuated PPL and improved peripheral arterial stiffness [115]. Additionally, combined walking and light RE performed 1 h after a high-fat meal attenuated PPL and, interestingly, more so compared to the same exercise performed 1 h pre-meal [66].

#### Exercise training

Findings show that the effect of exercise on PPL is an acute one [7], in contrast to its well-established chronic effect on fasting TAG concentration [116]. While endurance-trained people generally have low PPL and rapid TAG clearance, this is quickly reversed in the absence of recent exercise [5]. Data from the last decade confirm that the attenuating effect on PPL is abolished 37 to 48 h after an exercise session [14, 34, 117]. Therefore, any effect of exercise training on PPL should be considered a chronic effect only if it is observed at least two days after the last exercise session. In this sense, findings of studies that investigated the effect of training on PPL by administering a test meal less than two days or on undisclosed time after the last exercise session [118–122] cannot be considered as reflecting chronic exercise effects.

No effect of training on PPL was found after four weeks of high-intensity interval training in healthy volunteers when the test meal was administered at least three days after the last exercise session [123]. Similarly, eight weeks of low-volume endurance training did not influence PPL two days after the last session [124]. Additionally, no difference in PPL one day after the last session was observed between physically active and inactive patients with CVD [125].

Finally, there does not appear to exist an additive effect of previous exercise sessions, performed on consecutive days, to that of the last session [41, 67, 126]. On the other hand, two studies that compared the postprandial TAG response to a high-fat meal between inactive adults and physically active adults, who had abstained from exercise for two days, reported lower PPL in the active groups [127, 128]. Overall, it is interesting to mention that most studies that focused on the effects of training found a decrease in baseline TAG, which by itself is fairly interesting in terms of cardiovascular risk.

Thus, the short answer to the title question of this section (when is it most effective to exercise to lower PPL?) is: Exercise lowers PPL most effectively when it is performed on the day preceding a high- or moderate-fat meal, and this effect lasts up to approximately two days.

### What is the preferred exercise to lower PPL?

The types of exercise examined in previous reviews include MICE, HIIE, RE and accumulating exercise in the form of several short bouts throughout the day [8–11, 129]. Below we review recent findings on this issue, as summarized in ► **Table 1**.

#### MICE

Walking, running or cycling for 30 to 90 min at intensities ranging from 45 to 70% of  $VO_{2peak}$  reduced PPL when performed on

- i. the day before a high-fat meal [14, 21, 28, 29, 33, 36, 39, 40, 42, 46, 49, 50, 53, 76, 77],
- ii. the day before a moderate-fat meal [54, 55, 57, 58] or
- iii. the day of a high-fat meal [25, 60, 61] and a moderate-fat meal [26].

On the contrary, there are studies showing no effect of MICE on PPL when performed on

- i. the day before a high-fat meal [23, 37, 73, 78, 79, 81, 83, 85],

► **Table 1** Numbers of studies on the effects of exercise on postprandial lipemia published from 2014 to present.

Type of exercise	Timing of exercise relative to the test meal	Effect		Percentage of studies showing a lowering effect
		Lowering	None	
Moderate-intensity continuous exercise	Previous day	19	8	70
	Same day	4	8	33
High-intensity interval exercise	Previous day	8	4	67
	Same day	2	1	67
Resistance exercise	Previous day	3	2	60
	Same day	1	1	50
Accumulating short bouts of exercise	Previous day	3	0	100
	Same day	3	7	30

- ii. the day of a high-fat meal [71, 93, 95–97] or
- iii. the day of a moderate-fat meal [60, 98, 99].

In addition, a study has found reduced PPL with MICE in metabolically healthy individuals but not in individuals with metabolic syndrome [59]. Regarding the issue of whether MICE intensity plays a role in the lowering of PPL, most findings show a positive association [10], although, in one study [38], both high- and moderate-intensity exercises of similar energy expenditure were found to reduce PPL without a difference between intensities.

#### HIIE

From data reviewed in 2015, it appears that supramaximal, low-volume HIIE can induce reductions in PPL, but findings are inconsistent [11]. On the contrary, all studies using submaximal, high-volume interval exercise showed reductions in PPL [11]. Studies published afterwards showed that HIIE in the form of running or cycling reduced PPL when performed on

- i. the day before a high-fat meal [22, 23, 37, 47, 48, 51, 52],
- ii. the day before a moderate-fat meal [58] or
- iii. the day of a high fat meal [60, 61].

On the contrary, there are studies showing no significant effect of HIIE on PPL when performed on

- i. the day before a high-fat meal [70, 80, 82, 87] or
- ii. the day of a high-fat meal [60].

Comparisons between HIIE and MICE have shown the former to be more effective in lowering PPL, even when it has a lower energy expenditure [10, 23, 37]. However, low-intensity intermittent exercise was less effective than MICE [130], suggesting that exercise intensity is more important than exercise mode in lowering PPL.

#### RE

Recent studies have shown mixed results regarding the effect of RE on PPL, since some have found a lowering effect when exercise was performed on the day before [35, 39, 43] or on the day of the test meal [62], while others did not find a lowering effect when exercise was performed on the day before [82, 84] or on the day of the test meal [98]. Additionally, combined strength and endurance exercise of either circuit (strength exercises alternated with running bouts) or traditional pattern (strength exercises followed by MICE) reduced PPL after a high-fat meal [32].

#### Accumulating short bouts of exercise throughout the day

Performing short bouts of exercise during the day provides an additional physical activity option to individuals with limited time or with limited capacity to engage in more structured forms of exercise [9]. Most of the evidence until 2013 [9] and afterwards [30, 56] shows that exercise accumulated in this way is as effective as continuous exercise in reducing PPL on the next day. This has also been found with cycling sprints spread over the day [44]. When short bouts of exercise are performed on the day of the meal(s), most studies find no effect on PPL [104–110], whereas some find a lowering effect [26, 63, 64].

Thus, the short answer to the title question of this section (what is the preferred exercise to lower PPL?) is: Although MICE, HIIE, RE and accumulating short bouts of exercise throughout the day are all effective in lowering PPL, submaximal, high-volume interval exercise seems to be superior.

## How does exercise reduce PPL?

The potential factors contributing to the reduction of PPL by exercise are a lower rate of appearance and a higher clearance of TAG-rich lipoproteins (that is, intestinally derived chylomicrons and hepatically derived VLDL) during the postprandial period. Let us consider the evidence.

### Lower rate of appearance of TAG-rich lipoproteins in the circulation

Exercise may lower the rate of appearance of TAG-rich lipoproteins in the circulation due to

- i. decreased VLDL secretion [8, 10],
- ii. decreased rate of appearance of chylomicrons [12] and
- iii. decreased incorporation of endogenous and meal-derived fatty acids into TAG-rich lipoproteins [62].

### Higher clearance of TAG-rich lipoproteins from the circulation

After a meal, chylomicrons compete with VLDL for clearance by lipoprotein lipase (LPL) residing on the capillary endothelium of extrahepatic tissues, particularly adipose tissue and skeletal muscle. Exercise possibly augments this process through

- i. increased whole-body postprandial fatty acid oxidation [2, 12, 30], which may create a steeper inward fatty acid gradient, thus augmenting TAG hydrolysis by LPL,
- ii. increased expression of the muscle LPL gene during 4–8 h post-exercise, which returns to baseline at about 20 h [131], thus fitting with the time frame of the effectiveness of exercise in reducing PPL,
- iii. increased muscle LPL activity [12],
- iv. increased affinity of large VLDL particles for LPL postprandially [46] and
- v. increased chylomicron clearance because of decreased VLDL secretion and, hence, lower competition for LPL [132].

The reader is referred to Figure 2 of Gill and Hardman [5] for a visual presentation of the potential mechanisms involved. It is possible that the contribution of each of the aforementioned mechanisms to the PPL-lowering effect of exercise differs according to the time between exercise and meal, as well as the type of exercise. Thus, because activation of muscle LPL peaks at about 8 to 18 h post-exercise [131, 133], this is probably the main mechanism of PPL reduction in studies in which exercise was performed on the day preceding the meal, whereas decreased VLDL secretion is probably the main cause of PPL reduction when exercise precedes the meal by fewer than 3 h [132]. Additionally, studies using MICE suggest that reduced VLDL secretion may be more important than increased LPL activity and/or mass in PPL reduction [134], whereas evidence suggests that HIIE elicits PPL reduction mainly by increasing skeletal muscle LPL activity and/or mass [11, 135].

Thus, the short answer to the title question of this section (how does exercise reduce PPL?) is: Exercise reduces PPL by both lowering the rate of appearance and increasing the clearance of TAG-rich lipoproteins from the circulation.

## Conclusions

Most of the recent research reviewed in this paper strengthens previous findings regarding the effect of exercise on PPL, with new results mainly in the areas of exercise timing relative to meal(s), effectiveness of modern types of exercise and more real-life situations. Our main conclusions are:

- The adoption of exercise as part of an individual's daily routine results, among many other well-documented health benefits, in lowering PPL, thus reducing an independent risk factor for CVD.
- Evidence shows that exercise achieves this by both lowering the rate of appearance and increasing the clearance of TAG-rich lipoproteins from the circulation.
- The exercise-induced attenuation of PPL is lost after approximately two days; therefore, one should exercise frequently to maintain this benefit.
- Exercise is most effective in lowering PPL when performed on the day preceding a high- or moderate-fat meal. However, the time of exercise relative to a meal is not that important in real-life conditions, since one consumes several meals during the day; thus, an exercise bout will inevitably exert its lowering effect on PPL in one of the meals that will follow.
- Although MICE, HIIE, RE and accumulating short bouts of exercise throughout the day are all effective in lowering PPL, submaximal, high-volume interval exercise seems to be superior as long as it is tolerable.

## Recommendations for future research

Future research may focus on the following issues:

- Exploring the effect of exercise on PPL under more ecologically relevant dietary conditions, that is, moderate-fat, healthy meals (rather than high-fat meals) spread throughout the day.
- Monitoring lipemia through longer periods of the day (and, preferably, throughout 24 h) by taking advantage of modern blood microsampling techniques that do not require visits to the laboratory.
- Examining the effect of exercise on PPL within a more extended time frame (e.g., weekly), in which exercise bouts are mixed with meals, for gaining a more complete picture of the interplay between exercise and food consumption on lipemia.
- More balanced representation of females in studies assessing the effect of exercise on PPL.
- Examination of whether exercise performed and/or meals taken at different times of the day have different effects on PPL.
- Investigation of the physiological and biochemical mechanisms of PPL responses to exercise and diet.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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