Effects of brisk walking and green tea extract ingestion on lipid profile, aerobic capacity and physical fitness function in overweight and obese men

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Doctoral Thesis

Effects of brisk walking and green tea extract ingestion on lipid profile, aerobic capacity and physical fitness function in overweight and obese men

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Abstract

Background: The prevalence of overweight and obesity has increased dramatically over the last four decades. Excess weight is a well-recognized risk factor for several common chronic conditions including type 2-diabetes, metabolic syndrome, cardiovascular disease, and other health problems. Increased physical activity is an essential component of lifestyle intervention for obesity management and health improvement. Studies suggest the beneficial effects of green tea extract (GTE) for chronic diseases. In addition, studies in animal models reported that green tea catechins have a potential effect on endurance capacity. The effects of green tea combined with exercise on overweight and obesity may be a more effective means for the improvement of chronic diseases. However, the effects of GTE combined with aerobic exercise on lipid profile, liver function and physical fitness is not clear. Therefore, I hypothesized that GTE combined with brisk walking might improve the lipid profile, liver function, aerobic capacity, and physical fitness function in overweight and obese men, especially those with under uncontrolled dietary condition.

Methodology: This study investigated the effects of GTE combined with brisk walking in inactivity overweight and obese men. Twenty-four overweight or obese, non-smoking, males (39.8±8.8 years) volunteered for this study. None were regular consumers of green tea, exercise training. All subjects in the GTE group (n=12) or placebo group (n=12) attending the 12-week intervention program, and were followed

for 4 weeks post-intervention. In the intervention period, all participants were asked to consume two GTE (300mg EGCG) or placebo tablets daily. The exercise program involved 12 weeks of brisk walking at an intensity of 65%-80% of the maximum heart rate, which was supervised by heart rate belt. The brisk walking program consisted of four 60-min sessions per week, 12 weeks, each including a 5 min warm-up and 5 min cool-down. The intention-to-treat (ITT) efficacy analysis was used in this study. If data were not normality distributed, a Wilcoxon test was used within groups. To examine changes within and between groups after the intervention, we used analysis of co-variance (ANCOVA) to analyze the changes in outcomes between groups, and repeated measure analysis of variance was used to analyze the three times data.

Results: In the first study (chapter 2), after 12 weeks intervention, GTE group resulted in a significant decrease in the low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC) levels when compared to placebo group ($P < 0.01$). There was no significant change in the triglyceride (TG) or high-density lipoprotein cholesterol (HDL-C) levels in the placebo group, but a significant reduction was noted in the HDL-C levels in the GTE group ($P < 0.05$). There was also a significant reduction in the aspartate aminotransferase (AST) levels ($P < 0.05$) in the GTE group, but no change in the placebo group ($P = 0.162$). After 4 weeks follow-up period, there was a down trend in all parameters in both groups.

After 12-week intervention, the second study (chapter 3) showed that the combination effects of GTE and brisk walking has no significantly change in body weight, BMI, systolic blood pressure, and diastolic blood pressure in overweight and obese men. There was a significant reduce in waist circumference for the GTE group, no significant change in the placebo group. However, contrast to our hypothesis, we found a significant increase in fasting glucose levels in both groups after intervention.

In the third study (chapter 4), we found a significant increase in the aerobic capacity (6 min walking test) in both groups ($P<0.05$), and a significant change was found in the handgrip strength of the GTE group ($P<0.05$). After intervention, we found a significant decrease in time of the 8-foot up-and-go in both groups, and a significant increase in the length of sit and reach in both groups ($P<0.05$). While there was no significant change in the one-leg standing with eyes closed results of both groups. A down-ward trend was observed in the aerobic capacity and physical fitness function parameters after 4 weeks of follow-up.

In summary: GTE combined with brisk walking exhibited significant LDL-C and TC levels lowering properties in the overweight and obese men and also showed more effective improvement the liver function than brisk walking alone. This study provides data to support the main mechanism of action for the improvement of lipid profile by GTE. The mechanism underlying the reduction in plasma cholesterol levels by GTE might involve EGCG preventing the absorption of lipids and inhibiting digestive enzymes, with additional effects on the intestinal microbiota. Previous studies reported that exercise was able to improve the HDL-C and TG levels in human. However, we found a negative result in HDL-C levels in the GTE group and no significant change in the TG levels in both groups, which should be revealing the mechanism in the future studies. We found a significant increase in the handgrip strength in the GTE group, but no significant change in the placebo group. The results agree with a recent study, which showed that GTE combined with exercise was able to increase fatty acid oxidation in skeletal muscle and improve endurance capacity. The present doctoral thesis provides data to support the positive effects of green tea combined with brisk walking on lipid profile, liver function, aerobic capacity and physical fitness in inactivity overweight and obese men with under uncontrolled dietary.

Further studies on the effects of exercise intensity, dietary modification and the daily-dose of GTE are needed to clarify the effects of GTE combined with brisk walking in overweight and obese adults. Furthermore, an increased number of physiological parameters (maximal oxygen consumption, bone mineral density, body fat, muscle strength etc.) should be used in a future study to confirm the effects on physical fitness function.

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List of papers

This doctoral thesis consists of the following original publications:

Tengfei ZHANG, Si Chen, Atsushi SAITO. Effect of brisk walking on the body weight, body fat, waist circumference and blood lipids in adults: A systematic review. Journal of Health Science, 2019; 41; 23-39.

Tengfei ZHANG, Si CHEN, Atsushi SAITO. Effects of green tea combined with physical activity on blood lipids in humans A meta-analysis. Revista Brasileira de Medicina do Esporte(RBME), 2020, in press.

Tengfei ZHANG, Ningxia LI, Si CHEN, Zhenqing HOU, Atsushi SAITO. Effects of brisk walking combined with green tea extract on the aerobic capacity and physical fitness function in overweight and obese men: A randomized, double-blind, placebo-controlled trial. Advances in Physical Education (APE), 2020; in press.

Tengfei ZHANG, Ningxia LI, Si CHEN, Zhenqing HOU, Atsushi SAITO. Effects of green tea extract combined with brisk walking on lipid profiles and the liver function in overweight and obese men: A randomized, double-blinded, placebo-control trial. ANAIS DA ACADEMIA BRASILEIRA DE CIENCIAS, 2020; in press.

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Abbreviations

METs: metabolic equivalents

CVD: cardiovascular disease

T2DM: type 2 diabetes mellitus

LDL-C: low-density lipoprotein cholesterol

HDL-C: high-density lipoprotein cholesterol

TC: total cholesterol

TG: triglyceride

FG: fasting glucose

BMI: body mass index

BW: body weight

WC: waist circumference

RCT: randomized control trial

EGCG: Epigallocatechin gallate

EGC: epigallocatechin

ECG: epicatechingallate

EC: epicatechin

GTE: green tea extract

SMD: standardized mean difference

95% CI: 95% confidence interval

WHO: world health organization

CGSS: Chinese General Social Survey

NAFLD: non-alcoholic fatty liver disease

ALT: alanine transaminase

AST: aspartate aminotransferase

TBIL: total bilirubin

GGT: γ-glutamyl transpeptadase

FG: fasting glucose

SBP: systolic blood pressure

DBP: diastolic blood pressure

ECOLS: eyes closed and one-leg-standing

6MWT: 6 minutes walking test

SR: sit and reach

8FUG: 8-foot up and go

HS: handgrip strength

Chapter 1. Review of Literature

1. Overweight and obesity

The prevalence of overweight and obesity has increased dramatically worldwide. in 2016, the World Health Organization (WHO) classified 650 million adults (≥18 years) as obese (body mass index [BMI] $\geq$ 30 kg/m^2) and 1.9 billion as overweight (25 $\leqq$ BMI $<$ 30 kg/m^2) worldwide (Sibuyi, et al. 2018). The prevalence of overweight and obesity has become a fast growing epidemic among developed, developing and least developed countries (Malik, et al. 2013). The dramatically increased in obesity has been a risk factor for health impairment and threaten to reduce the physical fitness function in daily life and the length of life (Pataky, et al. 2014). Excess body weight or waist circumference is one of several risk factors for cardiovascular diseases, metabolic syndrome, type 2 diabetes mellitus, hyperlipidemia, and some cancers (Emanuela, et al. 2012, Ghoorah, et al. 2016, Seidell, et al. 2015, Vucenik, et al. 2012). Obesity also has a negative effect on economic. Study estimated that about $84 billion could be lost due to obesity-related chronic diseases in low-income and middle-income countries (Malik, et al. 2013). The WHO defines overweight and obesity as BMI $\geq$25 kg/m^2 and BMI $\geq$ 30 kg/m^2, which based on the data from whites. However, this criterion was not applicable to Asian. Therefore, based on Asian physical characteristics, (Jih, et al. 2014, Zeng, et al. 2014), the standard BMI cut points is that 23 - 27.5 kg/m^2 as overweight and $\geq$ 27.5 kg/m^2 as obese were chose for the Asian.

1-1. Overweight or obesity and lipid profile

In 2015, study reported that cardiovascular disease (CVD) was the leading cause of deaths worldwide, 65.3% BMI- related deaths were due to overweight and obesity (Afshin, et al. 2017). Additionally, dyslipidemia, high blood pressure and high fasting plasma glucose were identified more in overweight or obesity than normal subjects, particular in individuals whom intra-abdominal fat accumulation or a large waist circumference (Han, et al. 2016). Compared with normal body weight subjects, overweight and obesity is associated with high levels of low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), fasting glucose (FG), and triglyceride (TG) levels, and low levels of high-density lipoprotein cholesterol (HDL-C) (Klop, et al. 2013). The LDL-C, HDL-C, TG, and TC levels are important risk factors for the development of CVD and dyslipidemia. Studies (Casavalle, et al. 2014, Kang, et al. 2016, Reuter, et al. 2016) confirmed that significant correlation between dyslipidemia and overweight or obesity. Dyslipidemia, which is defined as reduce of HDL-C levels, or an increase in the TG or LDL-C levels, and also included an increase of plasma TC levels. These indices were primary risk factor for CVD. Obesity is a chronic metabolic disorder influenced by several factors such as lifestyle, behavioral, environmental, genetic susceptibility and family history. However, high energy food intake and inactivity were the important factors (Wang, et al. 2014). The guideline for management of obesity is that lifestyle changes, dietary modification, increased physical activity, use medication, and some serious patients for recommendation for surgery (Bray, et al. 2016). Regular physical activity could increase endurance and muscle strength, and then improve CVD in obesity (Thompson, et al. 2003). In addition, studies identified that physical activity combined with dietary modification or diet supplement have a significant effect on weight loss and lipid profile in overweight and obese human (Kelley, et al. 2012, Yuan, et al. 2018).

1-2. Obesity and physical fitness function

As the largest global chronic disease, obesity is not only a major risk factor for cardiovascular disease, but also a threat to cardiorespiratory capacity, balance, muscle strength and other physical fitness function (Capodaglio, et al. 2010). Overweight and obesity lead to a high incidence of early knee osteoarthritis; endurance induced, and limited flexibility of spine in these subjects (Gilleard, et al. 2007, Hue, et al. 2007). Excessive weight also changed the obesity patients' posture, which results in increased the risk of falling (Teasdale, et al. 2007). In addition, due to the body mass increased, the obesity patients' cardiopulmonary system metabolic was changed. This was results in these subjects were not seem capable of meeting cardiorespiratory metabolic, especially for sustained exercise or working (Capodaglio, et al. 2010). On the other hand, studies (Wee, et al. 2011, Xu, et al. 2008) have found negative consequences of obesity on muscle strength, which is associated with physical fitness function capacity decline, such as: lower walking speed, limited balance control and higher risk of falling than normal body weight subjects.

2. Walking and obesity

Obesity is a well-recognized risk factor for several common chronic conditions, such as CVD, type 2-diabetes, metabolic syndrome, cancer and other health problems (Afshin, et al. 2017). Study found a significant correlation between obesity and these chronic diseases. Increased physical activity not only maintains or reduction the body weight, but also reduction the risk of CVD. WHO recommended that 150 minutes of moderate intensity physical activity per week to reduce the risk of cardiovascular disease, metabolic syndrome, diabetes mellitus and all-cause mortality (Mendis, et al. 2015). Walking has been described as a near perfect exercise and recommended by all governments worldwide. The characteristics of walking are that simple, no special skills and safety, and walking also are the most commonly accepted in adults. Despite walking have a beneficial effect on health in inactivity or overweight and obesity subjects, however, studies confirmed that moderate-intensity or moderate to vigorous-intensity physical activity could significant improve the health condition in humans. Brisk walking, which defines as walking at a speed of 2.5 to 4.2 mph on firm ground, or with a total of 3100 - 4000 steps, or keep the maximum heart rate between 65% to 80% in walking period (Kearney, et al. 2014, Mabire, et al. 2017).

2-1. Walking and physical fitness function

Overweight and obesity affects physical fitness function linearly with the increase of BMI. Studies found that obesity has several negative effects on physical fitness function in these subjects. Obesity reduced the subjects' cardiorespiratory capacity, and static balance ability, which increased the risk of falling. A systematic review and meta-analysis (Hanson, et al. 2015) reported that walking could improve the cardiorespiratory capacity in adults. However, due to only two studies were included, and the results should be interpreted with prudence. Study by Blain et al. (Blain, et al. 2017) showed that 6 months walking program could significant change in endurance capacity in overweight and obesity older women. In another study, 13 weeks and 40 minutes four times weekly brisk walking increased the peak VO_2 and lower limb strength in middle-age women, which improved their physical fitness function (Kukkonen-Harjula, et al. 2007). Study by Kearney et al. (Kearney, et al. 2014) reported that 15 days walking intervention have a significant effect on handgrip strength and postural stability in overweight and obesity women. Similar to these studies, Kang et al. (Kang, et al. 2016) found a beneficial effect on balance and cardiorespiratory capacity in stroke patients. However, the effects of green tea and/or brisk walking on aerobic capacity or other physical fitness parameters were not clear in human study.

3. Effect of brisk walking on the body weight, body fat, waist circumference and blood lipids in overweight and obese adults: A systematic review

3-1. Introduction

It is widely assumed that regular physical activity can help prevent primary and secondary chronic diseases (Warburton, et al. 2016). Most countries' government and health organization recommend that subjects engage in regular moderate or vigorous intensity physical activity. However, modern society has changed our approach to work, and the modern lifestyle has also changed our behaviors. Whether working or enjoying leisure time, we spend a great proportion of our life engaged in sedentary behavior. Sedentary behavior is defined as any waking behavior characterized by an energy expenditure (as well as postural 「sitting or reclining」 and contextual 「waking」) ≤1.5 metabolic equivalents (METs) (Owen, et al. 2010). According to this definition, a person may be described as sedentary if they engage in a large amount of sedentary behavior. However, there was different energy expenditure in sedentary. For example, sitting in a classroom is assigned 1.8 METs, while driving a car is assigned 2.5 METs. There is no consistent definition of sedentary behavior; nevertheless, a common phenomenon exist namely a lack of ambulatory movement in any posture. This is an important characteristic that distinguishes sedentary behavior from physical activity. Physical activity is defined as any body movement generated by the contraction of skeletal muscles, such activity should increase energy expenditure above the resting metabolic rate. Physical activity is characterized by its modality, frequency, intensity, duration, and context of practice (Thivel, et al. 2018). A number of studies have found moderate-to-strong evidence that diabetes and mortality are associated with sedentary behavior (Proper, et al. 2011, van Uffelen, et al. 2010). Warren, et al. (Warren, et al. 2010) found that sedentary behavior was significant predictors of mortality due to cardiovascular disease (CVD). A review study showed that increased physical activity helps prevent chronic disease and promote public health (Haskell, et al. 2009).

Sedentary behavior is a major factor that increases the risk of chronic diseases, and it also significantly affects on one's body weight. Over the last three to four decades, the prevalence of overweight and obesity has increased dramatically. For instance, in 2015, about 107.7 million children and 603.7 million adults were obese around the world. Obesity is a major risk factor for CVD, type 2 diabetes mellitus (T2DM), hypertension, coronary artery diseases, metabolic syndrome, and some cancers (Malik, et al. 2013). It is also an important risk factor for death due to non-communicable disease.

Over nutrition is an obvious candidate contributor to the rise in obesity, but increased rates of physical inactivity and sedentary behavior are also implicated. Several studies have found that regular moderate physical activity was able to improve blood lipids, reduce the risk of CVD diseases, and prevent and control T2DM. It is also a good method of managing obesity. The World Health Organization (Committee. 2010) recommends that adults spend at least 150 minutes per week engaged in aerobic physical activity (moderate intensity) per week, or at least 75 minutes of high-intensity physical activity. The American College of Sports Medicine has similar recommendations in its physical activity guidelines.

Walking has been described as a near perfect ‘‘exercise’’ and has been recommended by health organizations worldwide (Morris, et al. 1997). Walking programs have a higher level of adherence than other forms of exercise (Siegel, et al. 1995). Brisk walking as a simple, economic and safe form of exercise is the most popular moderate-intensity aerobic physical activity for both men and women, especially for most middle-aged and/or overweight and obesity individuals. It is the most likely exercise or physical activity to be chosen to improve chronic diseases, and

T2DM and to manage body weight (Lee, et al. 2008). According to the definition of moderate-intensity activity, walking is ‘‘brisk’’ at a speed of 2.5 to 4.2 mph on firm ground. Studies have shown that 30 minutes of moderate-to-vigorous walking corresponds to a total of 3100 - 4000 steps (Pillay, et al. 2014). Previous studies have demonstrated that brisk walking can result in improved low density lipoprotein cholesterol (LDL-C), total cholesterol (TC) (Pagels, et al. 2012), and high-density lipoprotein cholesterol (HDL-C) (Murphy, et al. 2000). However, conflicting results have also been reported, with some studies showing that brisk walking has no substantial effect on the blood lipid values (Murtagh, et al. 2005, Tully, et al. 2005), although a systematic review and meta-analysis showed that brisk walking was able to significantly reduce the body weight, body mass index (BMI), waist circumference, and fat mass in obese subjects (Mabire, et al. 2017). Brisk walking proved to be an economic and feasible form of exercise that can be performed by nearly all individuals (especially for those with overweight and obesity), in all kinds of places and at almost any time.

The aim of this system review was to systematically summarize, analyze, and interpret the health benefits of brisk walking in overweight and obese adults with regard to its effects on body weight, the BMI, waist circumference, HDL, LDL, TC, triglyceride (TG), and other health-related measures.

3-2. Method

3-2-1. Literature search strategy

This systematic review followed the Cochrane systematic review guidelines. The online database Web of Science and PubMed were evaluated through August 3, 2018, for relevant periodicals. The PICO patient, intervention, comparison, and outcome (PICO) approach was used in this review search strategy. Our search eliminated two sets of keywords using the Boolean operator ‘‘NOT’’, and combined two sets of keywords using ‘‘AND’’, with ‘‘OR’’ used to combine the keywords. Our keywords search strategy included both full and abbreviated terms as follows: brisk walking, adults, overweight, obese, body weight, waist circumference, BMI, LDL-C, TC, HDL-C, fat ratio, and TG. The search initially yielded 523 potentially relevant articles. The duplicate articles were removed based on titles and abstracts. Due to the number of results, a second researcher independently screened a random sample of 20% of the retrieved record, and completed the inclusion of articles (Figure 1).

3-2-2. Inclusion and exclusion criteria

A study was included if the following requirements were met: (a) subjects ⩾ 18 years old; (b) randomized control trial (RCT); and (c) brisk walking or moderate exercise evaluated. (d) overweight or obese (BMI⩾25kg/m^2). The exclusion criteria were as follows: (a) study period of less than 2 weeks; (b) subjects ⩽ 18 years; (c) no relevant results; (d) a Nordic walking study or walking program study (not brisk walking).

3-2-3. Assessing the quality

The quality of the studies was assessed using the Cochrane Risk of Bias Tool. The criteria included random allocation, blinding of supplement, outcome assessors and individuals, allocation concealment, use of an intention-to-treat analysis, and other biases. Two researchers assessed the studies, separately. If any differences in their findings were noted, the conflict was resolved by a discussion.

3-2-4. Data extraction

Two researchers extracted all relevant data independently. One author extracted the following data from the eligible articles: the first author and publication year, study design, intervention duration, participants, intervention characteristics, control group characteristics, exercise (volume and intensity), and outcomes of body weight, waist circumference, BMI, LDL-C, TC, HDL-C, TG.

3-3. Results

A total of 523 RCT studies were identified through initial searches. Following the removal of duplicates, titles, and abstracts were screened, resulting in 59 articles undergoing full-text screening for inclusion. Overall, 25 RCT articles were identified (Figure 1). We excluded 34 articles for the following reasons: 6 were testing studies; 17 were combined with other exercises; 8 did not include indices, and 3 had no sedentary control group. This review identified a total of 1345 individuals (brisk walking group, n= 736; control group, n= 609), investigating the long-term health effects of brisk walking. Mean research duration was 3 - 48 weeks. The health of participants varied among studies, including overweight and/or obese, T2DM, nonalcoholic fatty liver, physically deconditioned, hypercholesterolemic, and eumenorrheic patients. Two studies did not report the values of body weight, body fat or waist circumference. And nine did not report the values of LDL-C, HDL-C, TG or TC (Table 1).

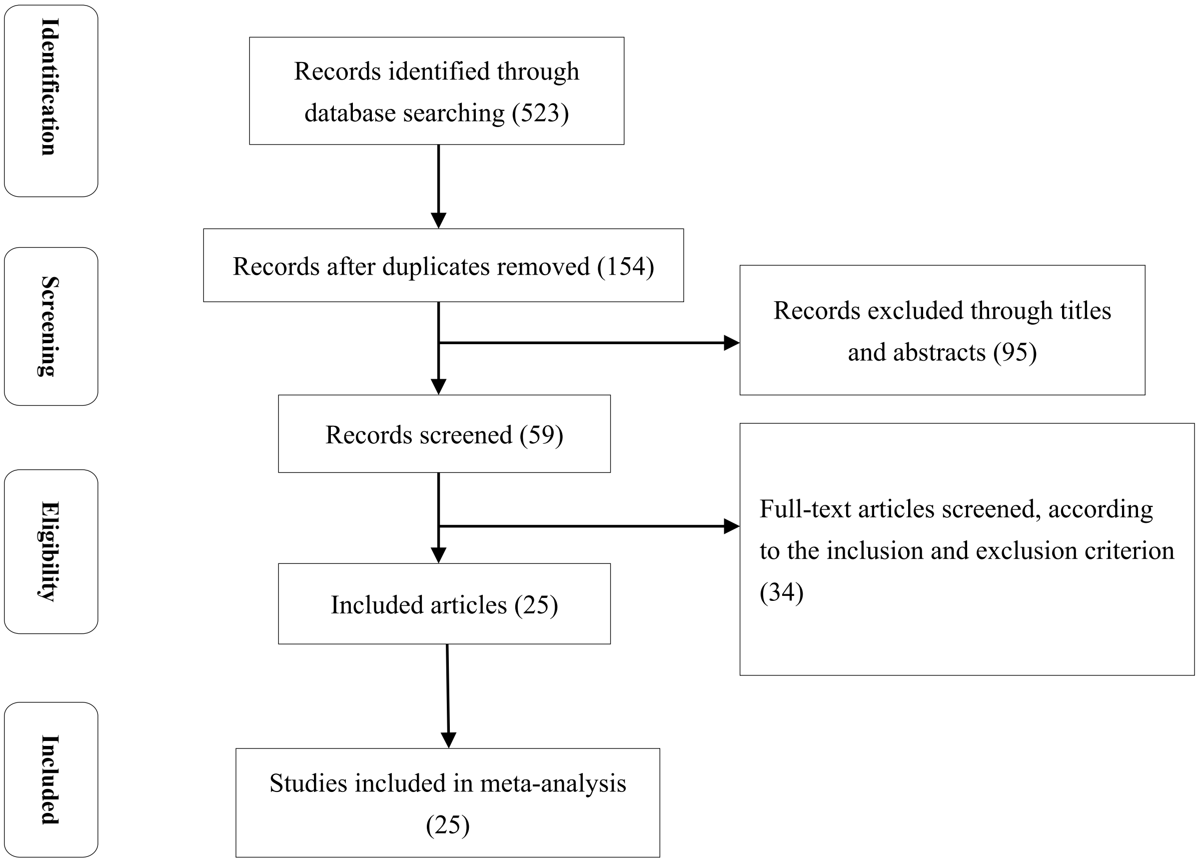


Figure 1 Flow diagram showing the literature search and selection process

Table 1 Basic characteristic of included 25 trials

Study	State of health	P	N	Age	BMI	Intervention	Ws	Intensity	Results physical fitness	Results blood lipids
Sylvia RC et al. (1991)	sedentary overweight and obesity	women	35	36.0 ± 1.6; 32.4 ± 1.5	28.3± 0.7 27.8± 0.9	IG=18, 45min/week, 5 time/week, 62±2% VO_{2max}; CG=17, habitual lifestyle	15	62±2% VO2max	BW none BF: none	unknown
John PF et al. (1993)	obesity	men and women	165	25~45	unknown	IG=43, 45min/time, 3~5 sessions/week, CG=38, habitual lifestyle	48	Self-monitoring ; breathing difficulty.	BW ↓ BF ↓ WC ↓	unknown
Stensel DJ et al. (1993)	sedentary healthy	men	72	42~59	25.3± 0.4 24.9± 0.6	IG=48, 20~25min to 40~45min/day, 2~3 sessions/week, CG=24, habitual lifestyle	48	self-monitoring	BW ↓ BF ↓ WC :none	HDL-C: none TC: none LDL-C：none TG: none
Aldred HE et al.(1995)	sedentary (overweight/ obesity)	women	26	41~55	unknown	IG=13, 60~180min/week, 3time/week, 20~50min/session , CG=13, habitual lifestyle	12	self-monitoring	BW ↓ WC :none	HDL-C: none TC: none LDL-C：↓ TG: none
Santiago MC et al.(1995)	sedentary eumenorrheic women	women	32	22~40	24.6± 3.8 23.6± 3.5	IG=21, 4.8km/week, 4time/week, mean intensity 72% maximal heart rate ; CG=11, habitual lifestyle	40	72% maximal heart rate	BW: none BF: none	HDL-C: none

Brooke-Wavell K et al.(1997)	sedentary post-menopausal women (health and overweight)	women	84	60~70	25.8± 3.8 25.6± 3.5	IG=43, 20~50min/day, 7time/week ; CG=41, habitual lifestyle	48	self-monitoring	BW ↓	unknown
Coleman KJ et al.(1999)	sedentary men (health and overweight)	men	36	18~45	25.0± 3.4 26.0± 4.5 26.4 ±4.1	IG1=12, 30min/day, 6time/week; IG2=12, 3×10min/day, 6 time/week; CG=12, self walk;	16	accelerometer	BW: none	unknown
Brooke-Wavell K et al. (2001)	Postmenopausal Women (overweight/ obesity)	women	68	60~70	unknown	IG=16, 120~280min/ two weeks, 3time/week, 20~45min/session ; CG=20, habitual lifestyle	48		BW ↓	unknown
Murtagh EM et al. (2005)	health overweight	men and women	30	45.7± 9.4	unknown	IG=8, 20min/day, 3 time/week; CG=7, habitual lifestyle;	12	heart rate; treadmill	BW: none BF: none WC: none	HDL-C: none TC: none LDL-C：none TG: none
Tully MA et al. (2005)	sedentary, overweight and obesity	men and women	31	50~65	28.09± 3.98 27.29 ±3.25	IG=17, 30min/day, 5 time/week; CG=9, habitual lifestyle;	12	self-monitoring	BW: none BF: none WC: none	HDL-C: none TC: none LDL-C：none TG: none
Audette JF et al. (2006)	sedentary; (health and overweight)	elderly women	27	71.4 ± 4.5	unknown	IG=10, 60min/day, 3 time/week; CG=8, habitual lifestyle;	12	maximal heart rate: 50%~70%	unknown	unknown

Lee MR et al. (2006)	overweight and obesity; high triglyceride	women	19	35 ~ 50	26.25± 1.83 26.53 ±1.38	IG=9, 20~50min/day, 3 ~6 time/week; CG=10, BW plus diet;	12	maximal heart rate: 40-50% ~ 60-70%	unknown	TG ↓
Kirkwood L et al. (2007)	overweight and obesity	women	69	30 ~ 50	31.6 ±3.8 31.6± 4.2	IG=19, 60min/day, 6 time/week; CG=18, habitual lifestyle;	12	accelerator monitors	BW ↓ BF ↓ WC ↓	HDL-C: none TC: none LDL-C：none TG: none
Tully MA et al. (2007)	sedentary (overweight and obesity)	men and women	106	40 ~ 61	27.79± 4.85 25.77± 4.09 26.32 ±5.94	IG1 =44, 30min/day, 3 time/week; IG2 =42, 30min/day, 5 time/week; CG=20, habitual lifestyle;	12	faster than normal, pedometer	BW ↓ BF ↓ WC ↓	HDL-C: none TC: none LDL-C：none TG: none
Coghill N et al. (2008)	hypercholesterolaemic (overweight and obesity)	men	67	55.1 ± 4.9	28.13 ± 3.86 27.27 ± 2.98	IG =38, 30min/day, 5 - 7 time/week; CG=29, habitual lifestyle;	12	accelerator monitors; RPE: 12 -14	BW ↓ BF ↓ WC ↓	HDL-C: none TC ↓ LDL-C：none TG ↓
Pagels P et al. (2012)	health	men and women	33	25 -45	26.2 ± 4.4 23.7 ± 2.3	IG = 16; 30 min/day, 7 time/week; CG=17, habitual lifestyle;	3	pedometer and accelerometer	BW ↓	HDL-C: none TC ↓ LDL-C ↓ TG：none

Foulds HJ et al. (2014)	health and overweight	men and women	72	44 ± 13.0	unknown	IG 1 = 10; 10min/week; IG 2 = 10; 10min/day, 3 time/week; IG 3 = 18; 30min/day, 3 time/week; IG 4 = 10; 60min/day, 3 time/week; CG=10, habitual lifestyle;	13	self-report	unknown	HDL-C ↑ TC: none LDL-C：none TG: none
Kearney TM et al. (2014)	sedentary; overweight and obesity	men and women	77	30 - 55	29.3 ± 4.3 29.2 ± 4.3	IG = 16; 3 × 10 min/day, 5 time/week; CG=17, habitual lifestyle;	24	self-report	BW: none BF: none WC: none	HDL-C: none TC: none LDL-C：none TG: none
Johnson ST et al. (2015)	Type 2 Diabetes	postmenopausal women	198	59.5 ± 8.3	34.6 ± 6.4 32.5 ± 6.4	IG = 102; 30 min/day, 3 time/week; CG=96, habitual lifestyle;	24	self-monitoring; pedometer	BW: none WC: none	HDL-C ↑ LDL-C：none
Zhang HJ et al. (2016)	Nonalcoholic fatty liver	men and women	220	53.9 ± 7.1	28.1 ± 3.3 28.0± 2.7	IG=73, 150min/week; CG=74, habitual lifestyle;	48	maximal heart rate: 45%~55%; pedometer	BW ↓ BF: none WC ↓	HDL-C: none TC: none LDL-C：none TG: none
Blain H et al. (2017)	sedentary and physically deconditioned	women	121	65.7 ± 4.3	24.25± 3.46 26.64 ± 4.22	IG=51, 150min/week, 3 time/week; CG=47, habitual lifestyle;	24	maximal heart rate: 40%~80%; HR monitor	BW ↓ BF: none	unknown
Buyukyazi G et al. (2017)	health	premenopausal women	30	33 - 50	23.6 ~ 29.6 20.9 ~ 30.1	IG=11, 30 - 51 min/week, 3 time/week; CG=8, habitual lifestyle;	8	maximal heart rate: 70%~75%; HR monitor	BW: none WC: none	unknown

Herzig KH et al. (2014)	health	men and women	78	58.8±10.4	32.6± 5.7 30.9 ± 4.8	IG=33, 60 min/week, 3 time/week; CG=35, habitual lifestyle;	12	3 ~ 5 km/h	BW ↓ BF ↓ WC ↓	HDL-C: none TC: none LDL-C：none TG: none
Ho SS et al. (2012)	overweight and obesity	men and women	81	40 - 66	32.7± 1.3 32.4 ±1.4	IG=15, 30 min/week, 5 time/week; CG=16, habitual lifestyle;	12	maximal heart rate: 60%±10%; treadmill	BW: none BF: none WC ↓	HDL-C: none TC: none LDL-C：none TG: none
McNeilly AM et al. (2011)	sedentary; obesity	men and women	24	54 ± 8	33 ± 6 32± 7	IG=12, 30 min/week, 5 time/week; CG=12, habitual lifestyle;	12	maximal heart rate: 65%; HR monitor	BW: none BF ↓ WC ↓	HDL-C: none TC: none LDL-C：none TG: none

LDL-C: low density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TC: total cholesterol; TG: triglyceride; BMI: body mass index; BW: body weight; WC: waist circumference; P: Participants; Ws: weeks; BF: body fat.

3-3-1. Brisk walking

The definition of brisk walking differed among the studies included in this review. Regarding the definition of brisk walking, the maximum heart rate ranged from 40% to 80%. Several studies were based on breathing difficulty, faster than normal, 62±2% VO_2max, 3~5 km/h. In addition, one study did not clearly define the meaning of brisk walking used in their trial. Eight studies reported that the definition of brisk walking was based on the participants' self reported description.

3-3-2. Effects of brisk walking on body weight and waist circumference

Four studies did not report the body weight. And 13 did not report waist circumference. Twelve studies included only women participants, 3 included only men, and 14 included both men and women participants. Thirteen studies (Aldred, et al. 1995, Blain, et al. 2017, Brooke-Wavell, et al. 1997, Brooke-Wavell, et al. 2001, Coghill, et al. 2008, Foreyt, et al. 1993, Herzig, et al. 2014, Hui, et al. 2016, Kirkwood, et al. 2007, Pagels, et al. 2012, Stensel, et al. 1994, Tully, et al. 2007, Zhang, et al. 2016) found a significant decrease in the body weight at the end of the study period. Twelve studies failed to show a significant decrease in the body weight, but seven of these trails included both men and women as participants; the physiology differs between sexes, which may have been a major confounding factor in our review. John's study, the first evaluated in this review, found that brisk walking significantly reduced the body weight in the intervention group compared with the control group. This was a long-term study, and the participants were sedentary obese women, however, the participants' BMI was not reported. Another study (Ohkawara, et al. 2007) showed that sedentary obesity and a long intervention period were important factors influencing the reduction in body weight. Figure 2 showed that no significant change on waist circumference in overweight and obese adults.

3-3-3. Effects of brisk walking on body fat

Seventeen trials measured the effect of brisk walking on body fat. Eight of these studies (AndreaM, et al. 2011, Coghill, et al. 2008, Foreyt, et al. 1993, Ho, et al. 2012, Hui, et al. 2016, Kirkwood, et al. 2007, Stensel, et al. 1993, Tully, et al. 2007) showed statistically significant decreases in body fat after intervention. However, there was no change in body fat (Figure 3).

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Coghill N 2008	100.47	8.46	38	100.44	7.81	29	21.5%	0.03 [-3.88, 3.94]
Herzig KH 2014	95.1	14.1	33	88.3	8.4	35	17.8%	6.80 [1.24, 12.36]
John PF 1993	103.27	14.53	26	106.2	13.74	26	13.6%	-2.93 [-10.62, 4.76]
Kirkwood L 2007	93.2	8.9	19	91.6	14.3	18	13.6%	1.60 [-6.12, 9.32]
McNeilly AM 2011	96.1	13.9	12	111.1	12.9	12	9.3%	-15.00 [-25.73, -4.27]
Murtagh EM 2005	84	12.5	15	83.7	9.3	7	11.0%	0.30 [-9.05, 9.65]
Pierce GL 2011	84.3	13.26	26	82.9	9.8	10	13.2%	1.40 [-6.53, 9.33]
Total (95% CI)			**169**			**137**	**100.0%**	**-0.14 [-4.19, 3.91]**

Heterogeneity: Tau² = 15.88; Chi² = 13.90, df = 6 (P = 0.03); I² = 57%

Test for overall effect: Z = 0.07 (P = 0.95)

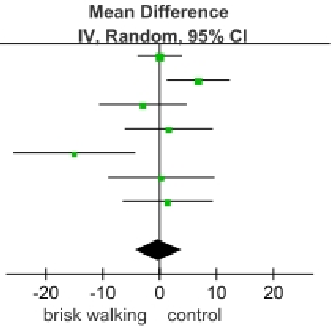


Figure 2 Effect of brisk walking on the waist circumference in overweight and obese adults

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Blain H 2017	34.41	5.46	51	36.18	4.17	47	13.0%	-1.77 [-3.68, 0.14]
Coghill N 2008	26.92	5.01	38	26.13	4.69	29	11.4%	0.79 [-1.54, 3.12]
Coleman KJ 1999	31.5	2.8	10	32.2	2.5	11	11.6%	-0.70 [-2.98, 1.58]
Herzig KH 2014	37.9	9	33	37.5	9.3	35	5.9%	0.40 [-3.95, 4.75]
Ho SS 2012	44.1	6.97	15	46.7	7.2	16	4.8%	-2.60 [-7.59, 2.39]
John PF 1993	31.38	4.59	27	29.19	5.86	26	9.6%	2.19 [-0.65, 5.03]
Kearney TM 2014	37.49	6.88	52	35.94	9.37	25	6.3%	1.55 [-2.57, 5.67]
Kirkwood L 2007	40	4.2	19	43.1	5	18	9.2%	-3.10 [-6.08, -0.12]
McNeilly AM 2011	41.5	5.4	12	49.3	11.5	12	2.7%	-7.80 [-14.99, -0.61]
Murtagh EM 2005	26.6	7.8	15	28.9	7	7	3.2%	-2.30 [-8.82, 4.22]
Pagels P 2012	26	4.3	16	23.6	2.3	17	11.2%	2.40 [0.03, 4.77]
Pierce GL 2011	32.6	10.2	26	34.9	9.48	10	0.0%	-2.30 [-9.36, 4.76]
Santiago MC 1995	26.8	6.8	16	29	7.1	11	4.3%	-2.20 [-7.56, 3.16]
Sylvia RC 1991	36.3	4.24	18	34.3	7.01	17	6.8%	2.00 [-1.87, 5.87]
Total (95% CI)			**322**			**271**	**100.0%**	**-0.27 [-1.54, 1.00]**

Heterogeneity: Tau² = 2.29; Chi² = 22.54, df = 12 (P = 0.03); I² = 47%

Test for overall effect: Z = 0.42 (P = 0.68)

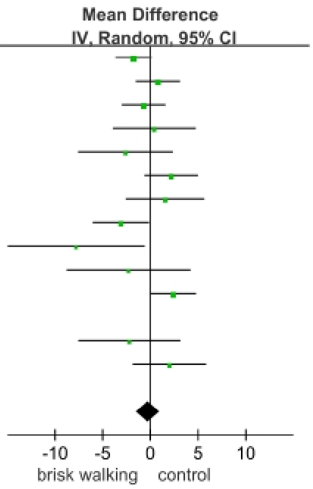


Figure 3 Effect of brisk walking on the body fat in overweight and obese adults

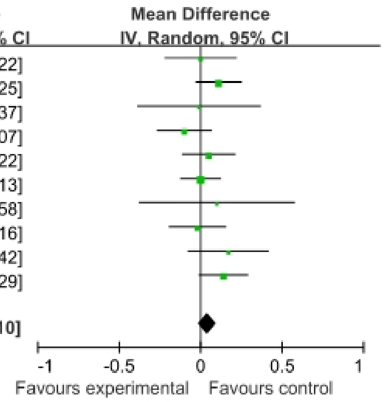
3-3-4. Effects of brisk walking on the LDL-C and TC levels

Seventeen trials measured the effect of brisk walking on the LDL-C and TC levels. Three of these trials (Aldred, et al. 1995, Higashi, et al. 1999, Pagels, et al. 2012) found statistically significant reductions in the LDL-C levels; however, one of these three studies included hypertensive participants, another had only a three-week intervention period and the third did not describe the BMI of the participants. Two (Coghill, et al. 2008, Pagels, et al. 2012) of seventeen studies shown a significant reduction in the TC levels; however, one of these two studies included hypercholesterolemic patients, and the other only had a three-week intervention period.

3-3-5. Effects of brisk walking on the HDL-C and TG levels

Nineteen trials measured the effects of brisk walking on the HDL-C levels. Four (Foulds, et al. 2014, Hardman, et al. 1989, Higashi, et al. 1999, Johnson, et al. 2015) of these studies reported that a significant increase in the HDL-C levels. However, the BMI of the participants was not mentioned in two of these studies, another included hypertensive participants, and the remaining one included type 2 diabetes patients. Seventeen trials measured the effect of brisk walking on the TG levels. Only two (Coghill, et al. 2008, Lee 2006) of these studies showed statistically significant reductions in TG. However, only two of these studies showed statistically significant reductions in the TG levels, with one including hypertensive subjects and the other one including high-triglyceride value subjects. There was no significant change in the

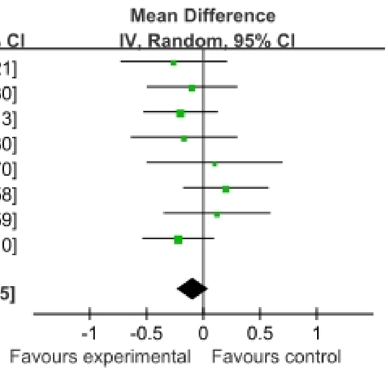
HDL-C and TG levels in overweight and obese adults (Figure 4 and Figure 5).



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Aldred HE 1995	1.57	0.29	13	1.57	0.29	13	6.6%	0.00 [-0.22, 0.22]
Coghill N 2008	1.51	0.31	38	1.4	0.28	29	16.2%	0.11 [-0.03, 0.25]
Foulds HJ 2014	1.4	0.3	18	1.41	0.57	10	2.3%	-0.01 [-0.39, 0.37]
Herzig KH 2014	1.4	0.4	33	1.5	0.3	35	11.4%	-0.10 [-0.27, 0.07]
Kearney TM 2014	1.4	0.29	52	1.35	0.37	25	12.0%	0.05 [-0.12, 0.22]
McNeilly AM 2011	1.1	0.1	12	1.1	0.2	12	20.4%	0.00 [-0.13, 0.13]
Murtagh EM 2005	1.5	0.6	15	1.4	0.5	7	1.4%	0.10 [-0.38, 0.58]
Pagels P 2012	1.3	0.21	16	1.32	0.3	17	10.5%	-0.02 [-0.20, 0.16]
Santiago MC 1995	1.65	0.37	16	1.48	0.29	11	5.2%	0.17 [-0.08, 0.42]
Stensel DJ 1993	1.49	0.42	48	1.35	0.24	24	14.0%	0.14 [-0.01, 0.29]
Total (95% CI)			**261**			**183**	**100.0%**	**0.04 [-0.02, 0.10]**

Heterogeneity: Tau² = 0.00; Chi² = 7.36, df = 9 (P = 0.60); I² = 0%
Test for overall effect: Z = 1.37 (P = 0.17)

Figure 4 Effect of brisk walking on the HDL-C levels in overweight and obese adults (mmol/L)



Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Coghill N 2008	1.74	0.74	38	2	1.12	29	9.2%	-0.26 [-0.73, 0.21]
Foulds HJ 2014	1.19	0.45	18	1.29	0.55	10	12.8%	-0.10 [-0.50, 0.30]
Herzig KH 2014	1.5	0.4	33	1.7	0.9	35	19.0%	-0.20 [-0.53, 0.13]
Kearney TM 2014	1.2	0.48	52	1.37	1.15	25	9.3%	-0.17 [-0.64, 0.30]
McNeilly AM 2011	1.8	0.8	12	1.7	0.7	12	5.6%	0.10 [-0.50, 0.70]
Murtagh EM 2005	1.2	0.6	15	1	0.3	7	14.4%	0.20 [-0.18, 0.58]
Pagels P 2012	1.25	0.8	16	1.13	0.55	17	9.2%	0.12 [-0.35, 0.59]
Santiago MC 1995	0.71	0.26	16	0.93	0.49	11	20.4%	-0.22 [-0.54, 0.10]
Total (95% CI)			**200**			**146**	**100.0%**	**-0.09 [-0.23, 0.05]**

Heterogeneity: Tau² = 0.00; Chi² = 5.12, df = 7 (P = 0.64); I² = 0%
Test for overall effect: Z = 1.23 (P = 0.22)

Figure 5 Effect of brisk walking on the TG levels in overweight and obese adults (mmol/L)

3-4. Discussion

The aim of this review was to assess the effect of brisk walking on the body weight, body fat, waist circumference, and blood lipid values in overweight and obese adults. A total of 25 intervention studies met the inclusion criteria and were included in this review. While all of the included trials assessed brisk walking as the modality, the intensity of the exercise varied widely. Brisk walking has been confirmed as a suitable activity for maintaining a healthy lifestyle by the world health organization, public health agencies, and health research institutions around the globe. However, the precise definition of brisk walking remains unclear. Porcari et al. (Porcari, et al. 1987) showed that brisk walking is defined as a maximal heart rate of ⩾ 70%. Spelman et al. (Spelman, et al. 1993) similarly suggested that the maximal heart rate should be above 70%. Previous studies (Pate, et al. 1995, Suter, et al. 1994) have shown that brisk walking is defined as a speed of walking ranging from three to four miles per hour.

However, only 7 trials in our review reported that a maximal heart rate ⩾70% was achieved. Other studies used self-monitoring to assess the presence of brisk walking (accelerator, pedometer and rate of perceived exertion scale). One of these studies reported that the maximal oxygen consumption should be 62% ±2% for brisk walking. Another study that assessed the speed and intensity of walkers showed that the threshold of maximal oxygen consumption was 68.6% ±14.9%.

A systematic review and meta-analysis (Mabire, et al. 2017) demonstrated that brisk walking was able to reduce the body weight, body fat and waist circumference in obese adults. Twelve studies in our review reported statistically significant changes in the body weight, and eight reported statistically significant changes in the body fat and waist circumference. The intensity of brisk walking differed markedly among our included studies. Nemoto et al. (Nemoto, et al. 2007) found that brisk walking, defined as a maximal oxygen consumption of 50% - 70%, was able to reduce the body mass. Blain et al. (Blain, et al. 2017) also showed that brisk walking, defined as a maximal oxygen consumption of 60% - 80%, was able to reduce the body mass and body fat of sedentary women. Maintaining or increasing the amount of moderate or vigorous intensity physical activity is recommended by a number of health organizations to reduce the risk of chronic diseases in sedentary adults. As the one of the most popular physical activities, brisk walking could reduction the body mass, body fat or waist circumference. However, the recommended levels of such physical activities have generally not led to clinically significant body mass loss (Donnelly, et al. 2000). Previous studies (Church, et al. 2007, Donnelly, et al. 2003) also have shown that statistically significant weight loss generally does not occur with moderate-intensity physical activity. However, it was able to change the other favorable cardiometabolic. Thus, while brisk walking can reduce body weight, no significant reduction in body weight may occurs.

Several studies have shown that physical activity has favorable effects on the blood lipid and lipoprotein profiles. A previous review (Durstine, et al. 2001) found that exercise increased the HDL-C levels and reduced those of TG and LDL-C. However, other studies on the effects of aerobic exercise on the lipids and lipoproteins in adults with cardiovascular disease have yielded conflicting results, with the changes in the blood lipid values not always being statistically significant. Indeed, only six trials among the studies included in our review reported statistically significant reductions in the blood lipid and lipoprotein values, and four of these studies included chronic disease patients as participants. Another meta-analysis showed that aerobic exercise increased the HDL-C and decreased the TG levels in adults, especially men, with cardiovascular disease (Kelley, et al. 2012). This finding, along with others, confirmed that physical activity could improve the blood lipid and lipoprotein levels. Physical activity can not only improve the health of chronic disease patients, but also reduce the risk of chronic disease altogether in healthy humans. A meta-analysis found that the effect of physical activity on blood lipids was associated with increased levels of such activity, and Duncan et al. (Duncan, et al. 1991) found that a difference in the amount of-exercise appears to result in a different outcome in the blood lipid values. Another study (Crouse, et al. 1997) showed that different intensity levels also significantly affected the lipoprotein levels.

In conclusion, present review found that a brisk walking program may reduce the body weight, body fat, and waist circumference, as well as reduce the levels of LDL-C, TC and TG, and increase the levels of HDL-C. Furthermore, two factors were found to influence the effects of brisk walking on the body weight, body fat, and waist circumference and blood lipids: (1) the amount and intensity of the brisk walking, and (2) the state of health of the participants.

Limitation

Several limitations associated with the present review warrant mention. First, our review was confined to published research, and we simply searched PubMed and Web of Science to find appropriate articles. Second, there may have been some bias in a few of the selected studies, which may have influenced the results. Finally, the health of the subjects among the different studies may have influenced the findings, including type 2diabetes mellitus, physically deconditioned, hypercholesterolemic, and eumenorrheic patients. Such limitations may thus have been major confounding factors in this review.

4. Green tea

Green tea dried leaves was unfermented made from plant of Camellia sinensis (L.), as a popular beverage in China, Japan, Korea, some parts of North Africa, which become more popular in the United States and Europe (Moore, et al. 2009). Green tea and/or green tea extract can help protect against chronic diseases, such as metabolic syndrome, type 2-diabetes, and CVD. Epigallocatechin 3 gallate (EGCG) is the most abundant and accounts for about 60% of green tea catechins (Sharma, et al. 2012).

4-1. Plausible mechanisms for the improvement of lipid profile by green tea or GTE

To studies date there are two major proposed mechanisms (Yang, et al. 2016) of action for green tea or GTE, one is that the green tea or GTE reduce the blood cholesterols levels, reduction and inhibition of cholesterol synthesis and absorption. The other one is that green tea constituents modulation the LDL-receptor and possible mediated by AMPK or other signal pathways. The mechanism of green tea or GTE effect on cholesterol has been studied in animals. For example, Bursill et al. (Bursill, et al. 2007) reported that 4 weeks of green tea and cholesterol-fed, modulation the LDL receptor and inhibiting cholesterol synthesis which results in lower the plasma cholesterol in rabbit. Grove et al. (Grove, et al. 2012) found that 6 weeks of dietary EGCG could modulation of lipid absorption via pancreatic lipase, and results in increased fecal lipid in high fat-fed obese mice. Furthermore, a recently study by Li et al. (Li, et al. 2018) found that EGCG had a significant effect on serum lipid metabolism and EGCG modulation the activation of AMPK in liver and skeletal muscle. In addition, the study also revealed EGCG could increase the excretion of free fatty acids from feces and inhibited the expression of genes. In human study, a previous study by Onakpoya et al. (Onakpoya, et al. 2014) reported that green tea ingestion results in significantly reduction in the LDL-C and TC levels in humans. Another systematic review and meta-analysis (Kim, et al. 2011) also found that green tea catechins has a positive effect on the LDL -C and TC levels in humans. However, there was no significant change in the TG and HDL-C levels in these studies.

4-2. Anti-obesity mechanisms of green tea extract

There are several possible mechanisms of green tea or GTE influence on body weight and body fat, and at least two major mechanisms (Moon, et al. 2007, Suzuki, et al. 2016) were included. Firstly, the underlying in weight loss mechanism of action of green tea or GTE is that after ingestion, GTE could inhibit the activity of digestive enzymes, prevention of absorption and also modification the intestinal microbiota.

The other mechanism is mediated through modification of preadipocyte, stimulation gene expression in adipose tissues and signal transduction in tissues.

The possible mechanisms of GTE influence on body composition have been found by animal studies, and also reported in the human studies. Unno et al. (Unno, et al. 2009) reported that 4 weeks of tea catechins was able to increase the fecal of ingestion energy nutrients in rats, which confirmed GTE inhibiting the digestive enzymes and prevention of nutrient absorption. Ikeda et al. (Ikeda, et al. 2005) reported that EGCG was able to inhibit the pancreatic lipase and results in slow down triacylglycerol absorption in rats. Study (Fei, et al. 2014) also found that EGCG exhibited inhibitory effects on pancreatic α-amylase in vitro. In human studies, Venables et al. (Venables, et al. 2008) found that acute ingestion GTE can increase fat oxidation during the aerobic exercise and also can improve the glucose tolerance in healthy young men. Study also (Park, et al. 2009) found that EGCG was able to inhibit the glucose transportation and absorption when co-ingested in human. Another study (Jarosław, et al. 2013), in subjects labeled mixed triglyceride breath test was performed twice with or without GTE. This study concluded that GTE can reduce the lipid digestion and absorption in humans.

4-3. Green tea or green tea extract and obesity

Epidemiological studies have reported that daily consumption tea could maintain or reduced the body weight. For example, an epidemiological study (Vernarelli, et al. 2013) found that regular consumed hot tea individuals had lower BMI and waist circumference than non-consumers, but the results was contrast to the adults who ingestion ice tea. Similar to these study findings, the other cross-sectional study (Grosso, et al. 2015) found that the subjects who daily ≥3 cups tea consumptions had lower BMI and waist circumference, and the study also reported tea consumption was negatively associated with fasting plasma glucose in women, but no relationship with men. On the other hand, intervention clinical studies also showed the beneficial effects of tea or tea extract on overweight and obesity. In an early double-blind randomized controlled study found that tea catechin-rich beverage could improve the serious obesity and cardiovascular disease risk factors for the obese or near-obese Japanese children (Matsuyama, et al. 2008). A similar result was drawn from the other clinical study (Brown, et al. 2011), which shown ingestion 800 mg of green tea catechins could decrease the body weight in overweight and obese men. Review (Suzuki, et al. 2016) reported that green tea or GTE has been showed a positive effects on anti-obesity.

5. Effects of green tea combined with physical activity on blood lipids in humans: A meta-analysis

5-1. Introduction

Green tea (Camellia sinensis), which contains several kinds of polyphenols, is one of the most popular beverages in the world. These polyphenols are classified into pyrogallol-type and non-pyrogallol-type catechins. Previous studies have reported four major catechins in green tea, (both pyrogalloland and non-pyrogallol-type catechins): Epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechingallate (ECG), and epicatechin (EC) (Braicu, et al. 2013, Du, et al. 2012, Kanwar, et al. 2012). EGCG is the most pharmacologically active of these catechins (Senanayake 2013). Study have shown that tea catechins can be used to help prevent various types of disease, describing their anti-bacterial, anti-obesity, anti-diabetic, and anti-cancer effects (Miyamoto, et al. 2017). The preventing of CVD is a major, important effect of GTE and can be largely attributed to EGCG, the major the most pharmacologically active component of tea catechins (Chen, et al. 2016).Several mechanisms through which green tea extract can reduce the risk of CVD have been suggested. One of the main mechanisms is the antioxidant effects, which prevent oxidative modification to LDL-C, which is an important step in the progression of atherosclerosis (Stangl, et al. 2007). A meta-analysis reported that the intake of GTE improved the lipid profile in humans, especially for LDL-C and TC (Pang, et al. 2016). Cardiovascular disease (CVD) alone accounts for 48% of Non-communicable diseases, which leading cause of death worldwide, and is expected to affect more than 23.6 million people by 2030 (Okwuosa, et al. 2016). CVD not only harms individuals but also places a heavy economic burden on governments around the world (Laslett, et al. 2012). The major risk factors for CVD include smoking, overall alcohol consumption, dietary cholesterol, hypertension, and diabetes mellitus (Nascimento, et al. 2014). Thus, controlling the risk factors for CVD is important for reducing its incidence. As a well-established risk factor of CVD, LDL-C has been key target in the treatment, control and prevention of CVD. In addition, lower levels of HDL-C, and higher levels of TC and TG have been associated with an increased risk of CVD (Piepoli, et al. 2016).

The European guidelines for the prevention of CVD suggest that nutrition supplementation and physical activity might be useful for preventing CVD and modifying an unhealthy lifestyle (Piepoli, et al. 2016). It is widely accepted that physical activity not only helps maintain or promote one's physical fitness but also reduces weight (Petersen, et al. 2004) and improves type 2 diabetes mellitus (Hu 1999), and cognition and health defects due to an unhealthy lifestyle across age groups (Reiner, et al. 2013). Physical activity also improves the serum lipid profile through mechanisms that increase the lipoprotein lipase activity in skeletal muscle, elevate HDL-C levels, and enhance the transport of plasma lipids and lipoproteins from the peripheral circulation and tissues to the liver (Park, et al. 2015). Numerous studies have shown that physical activity increases HDL-C levels and reduces the TG levels in adults, and the risk of CVD is reduced linearly with increased activity (Ahn 2016, Pattyn, et al. 2013). In addition, aerobic exercise increases the HDL-C content, while exercise reduces the LDL-C and postprandial TG levels, with a particularly significant effect on the HDL-C levels content (Tseng 2013). However, exercise in combination with green tea has shown a controversial result on the lipid and lipoprotein content. Although many systematic reviews and/or meta-analyses have summarized the effects of the consumption green tea on CVD and the total mortality, blood pressure, and lipid profile, there have no meta-analyses to assess the effects of GTE combined with physical activity on the serum lipid content. Thus, the aim of this meta-analysis was to compile evidence on the effects of physical activity combined with GTE on the serum lipids and lipoprotein content in humans.

5-2. Methods

5-2-1. Search strategy

This review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline, 2009. Three electronic databases (PubMed, Web of Science, and the Cochrane Library) were searched for articles written in English and published before June 2017, using the following combinations of text and medical subjects heading [MeSH] terms: “green tea extract” or “catechin” or “tea polyphenols” or “EGCG” or *Camellia sinesis* and “physical activity” or “exercise” or “walking” or “training” or “strength training” or “aerobic exercise” or “isometric exercises”; and “serum lipids” (“lipoproteins” or “high density lipoprotein cholesterol” or “HDL-C” or “low density lipoprotein cholesterol” or “LDL-C” or “total cholesterol” or “TC” or “triglyceride” or “TG”). Two reviewers independently searched the studies (ZHANG and CHEN).

5-2-2. Eligibility criteria

We included randomized controlled trial (RCT) investigating the effect of physical activity combined with GTE on the lipid profiles parameters (HDL-C, LDL-C, TG, and TC) in participants of both sexes. The inclusion criteria were as follows: studies should involve (1) physical activity combined with GTE ingestion; (2) randomized control trials; and (3) human research. The exclusion criteria were as follows: the trial (1) involved transient testing; (2) did not report at least one of HDL-C, LDL-C, TG, or TC; (3) had a study period of less than two weeks; (4) included other nutritional supplements combined with GTE.

5-2-3. Data extraction

Two researchers extracted all relevant data independently. One author extracted the following data from the eligible articles: first author and publication year, study design, intervention duration, participant (men and women), dose of GTE, intervention characteristics, control group characteristics, exercise (volume and intensity), and outcomes of HDL-C, LDL-C, TG and TC (mean standard deviation).

5-2-4. Quality assessment

The quality of the studies was assessed using the Cochrane Risk of Bias Tool. The criteria included random allocation, blinding of supplement, outcome assessors and individuals, allocation concealment, use of an intention-to-treat analysis, and other biases. Two researchers assessed the studies, separately. If any differences in their findings were noted, conflict was resolved by discussion.

5-2-5. Statistical analyses

We estimated the relationship between the GTE combined with physical activity group and the control group based on the data presented as the standardized mean difference (SMD). Mean changes in the LDL-C, TC, HDL-C and TG levels were used to first assess the differences between the trial and control groups. Due to the different units of measurement used in study, we converted all measures of mg/dl to mmol/L. We therefore used a random-effects model meta-analysis. Subgroup analyses (based the daily dosages of EGCG [≤ 150mg or >150mg] in trials, and based on the exercise intensity in studies) (Dekant, et al. 2017) were performed. $I^2$was used to assess heterogeneity between studies, and I^2 values of <25%, 25%-75%, and >75% were considered to indicate low moderate, and high heterogeneity, respectively. Egger's test was used to assess the publication bias (P<0.1 was considered to indicate significant publication bias). Statistical analyses were performed using the STATA version 15.0 software program (Stata Corporation, College Station, TX, USA). P values of <0.05 were considered to indicate statistical significance.

5-3. Results

The results of our electronic literature search and the study selection process are shown in Figure 6. We searched 271 articles and identified 31 potentially eligible trials. We included 7 of the RTC trials (Belcaro 2013, Gahreman, et al. 2016, Kajimoto, et al. 2003, Miyazaki, et al. 2013, Nagao, et al. 2007, Rostamian, et al. 2017, Stendell-Hollis, et al. 2010) that enrolled a total of 608 participants in the meta-analysis. All of the studies had a randomized design: four had a double-blind randomized design, one had a single-blind design, and two simply had a randomized design. Physical activity included aerobic exercise, and resistance training combined with aerobic exercise. Two studies used an activity level assessment. One study did not report the main component of GTE, and one used decaffeinated GTE. The participants in all of the RCTs were different, they included healthy subjects (two studies), obese subjects (two studies), overweight breast cancer survivors (one study), subjects with metabolic syndrome (one study), and subjects with hypercholesterolemia (one study). The characteristics of the patients that were evaluated in the meta-analysis are listed in Table 2.

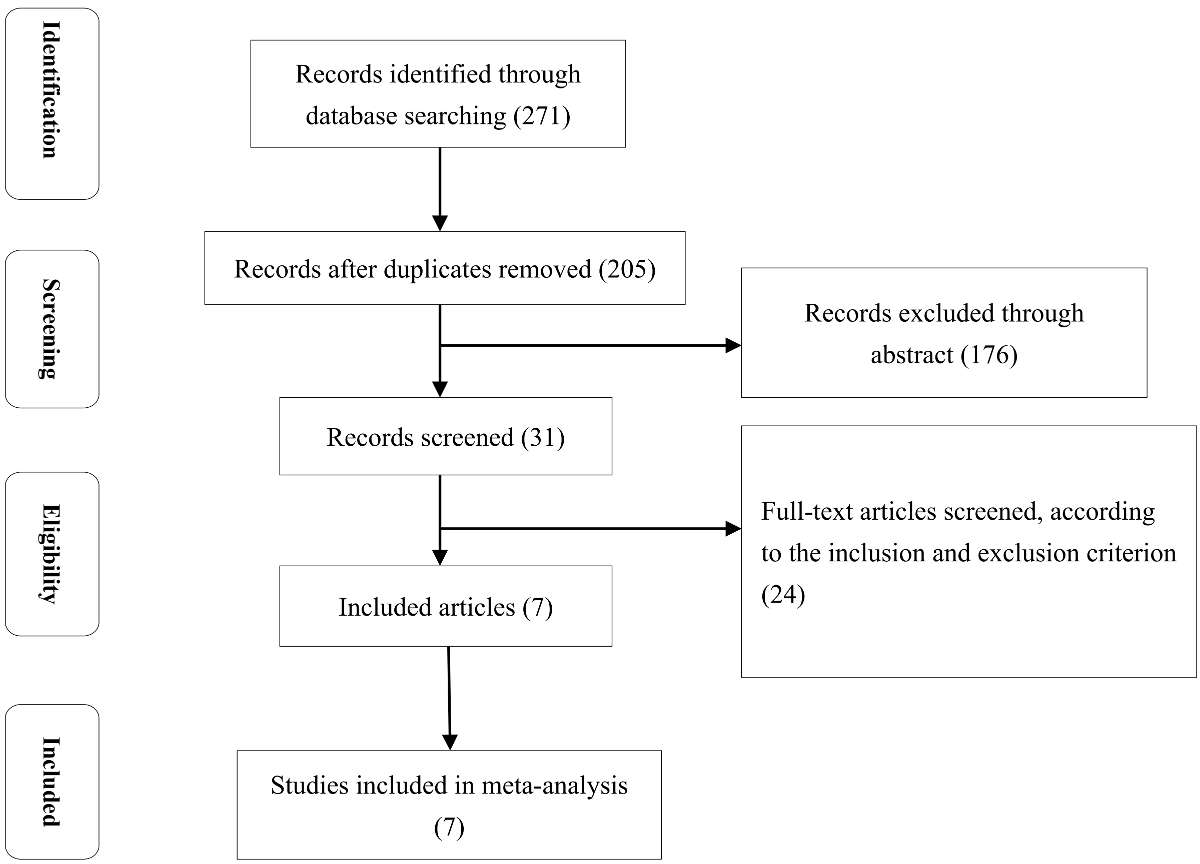


Figure 6 Flow diagram showing the literature search and selection process

Table 2 Basic characteristic of included 7 trials

reference	year	study design	Duration	P (N)	age(year)	GTE(mg)	Placebo(mg)	Density- exercise	health condition	lipids
Belcaro G et al	2013	randomized, single-blinded	24 W	male and female; 100N	47.6±5.5 C:45.3±3.5	300mg/d EGCG≥13% Ps:19%-25%;	Cellulose	70% moderate aerobic; 30% muscular strength	borderline metabolic syndrome	TG ↓ HDL-C↑
Rostamian M et al	2017	randomized	2 W	female; 24N	50-58	GTE: 1200	Cellulose	aerobic exercise 4 times/week; 40-50min/session	sedentary postmenopausal women	TG ↓ LDL-C↓ HDL-C↑
Nagao T et al	2007	randomized, double-blind, parallel	12 W	male and female; 270N	25-55	TCs: 583 Cs: 42.8 CG: 40.1GC: 127.5 GCG: 139.7 EG: 69.4 EGCG: 100.3	Cs: 100 Caffeine: 75	daily activity assessment	visceral fat-type obesity	LDL-C↓
Miyazaki R et al	2013	double-blind, placebo	14 W	male and female; 52N	69.1±5.9	TCs: 630.9 Cs: 30 CG: 24.8 GC:125.7 GCG:112.6 EG:45.8 EGCG: 143.2	TCs: 88.7 Caffeine: 82.4	walking	older people	TC ↓ LDL-C↓
Gahreman D et al	2016	randomized	12 W	male 48N	26.1±0.7	GTE: 750 Ps: 562.5 EGCG: 375	None	Interval spring exercise 3times/week	overweight men	none
Stendell-Hollis N.R et al	2010	randomized, double-blind	24 W	female; 54N	56.6±8.1 C:57.8±8.5	Cs: 235.64 EGCG：128.84	herbal tea	activity level assessment	overweight breast cancer survivors	HDL-C↑
Kajimoto O, et al.	2003	double-blind	12 W	male and female;60N	47.4±10	TCs:197.4 EGCG: 67.5 ECG: 25 GCG:82.5	Cyclodextrin	walking	hypercholesterolemia patients	TG ↓ LDL-C↓ HDL-C↑TC↓

TCs =total catechins; Cs =catechin; Ps = polyphenols; C =control; W =weeks; P =participants; N =numbers; GCG=Gallocatechin-3-O-Gallate; CG =Catechin-3-O-Gallate; GC = Gallocatechin

5-3-1. Effects of GTE on the LDL-C and TC levels

Three RCT studies reported that GTE combined with physical activity increased the level of LDL-C, and one showed significant effects in the GTE group in comparison to the placebo group. A meta-analysis of 6 trials (Figure 7) failed to show a significant decrease in the LDL-C level in the GTE group in comparison to the placebo group (SMD:-0.169; 95% confidence interval [CI]:-0.414 to 0.076; I^2=22.7%; p=0.177). A subgroup analysis revealed no significant differences in the LDL-C values between the subjects who received higher and lower doses of EGCG.A similar relationship was observed in the physical activity subgroup analysis. However, the heterogeneity in the higher-dose EGCG group was I^2=61.9% (p=0.105). Because only two studies were included, we were unable to perform a sensitivity analysis. According to Egger's test, there was no publication bias (p=0.895).

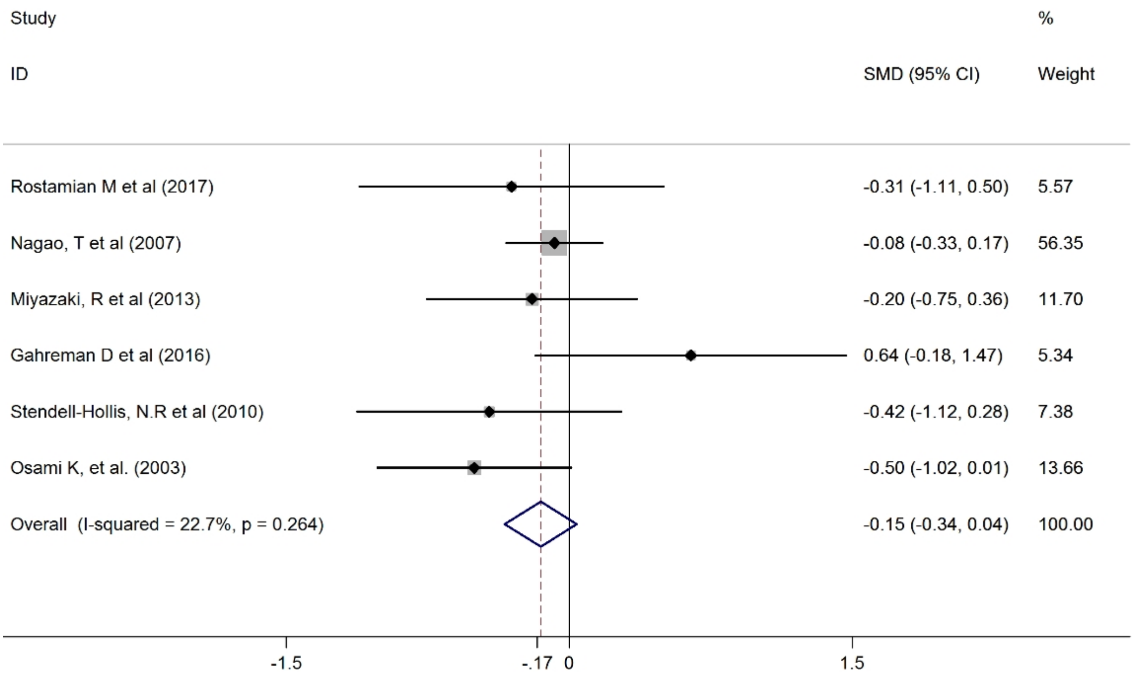


Figure 7 Results of evaluating the effect of GTE combined with exercise on LDL-C levels (mmol/L). Sizes of data markers indicate the weight of each study in the analysis.

Two trials reported a significant decrease in TC levels after intervention in the GTE plus physical activity group, while one showed a significant reduction in the placebo group. The results of a meta-analysis of all of the included studies showed that GTE combined with physical activity was not associated with the serum value of TC (SMD:-0.219; 95%CI:-0.533 to 0.094; I^2=48.1%; p=0.170). According to Egger's test, there was no publication bias (p=0.239). We divided the studies into subgroups for an analysis, and found non-significant decreases in the lower- and higher-dose GTE groups in comparison to the placebo group, with the same results obtained in the physical activity subgroups. Due to the higher heterogeneity in the subgroup analysis, we performed a sensitivity analysis by removing each study from the meta-analysis (SMD:-0.436; 95%CI:-0.770 to -0.102; I^2=0%; p=0.01) (Figure 8), significant decreases were noted in the lower-dose EGCG group and in the daily activity group (SMD:-0.594; 95%CI:-1.012 to -0.177; I^2=0%; p=0.005).

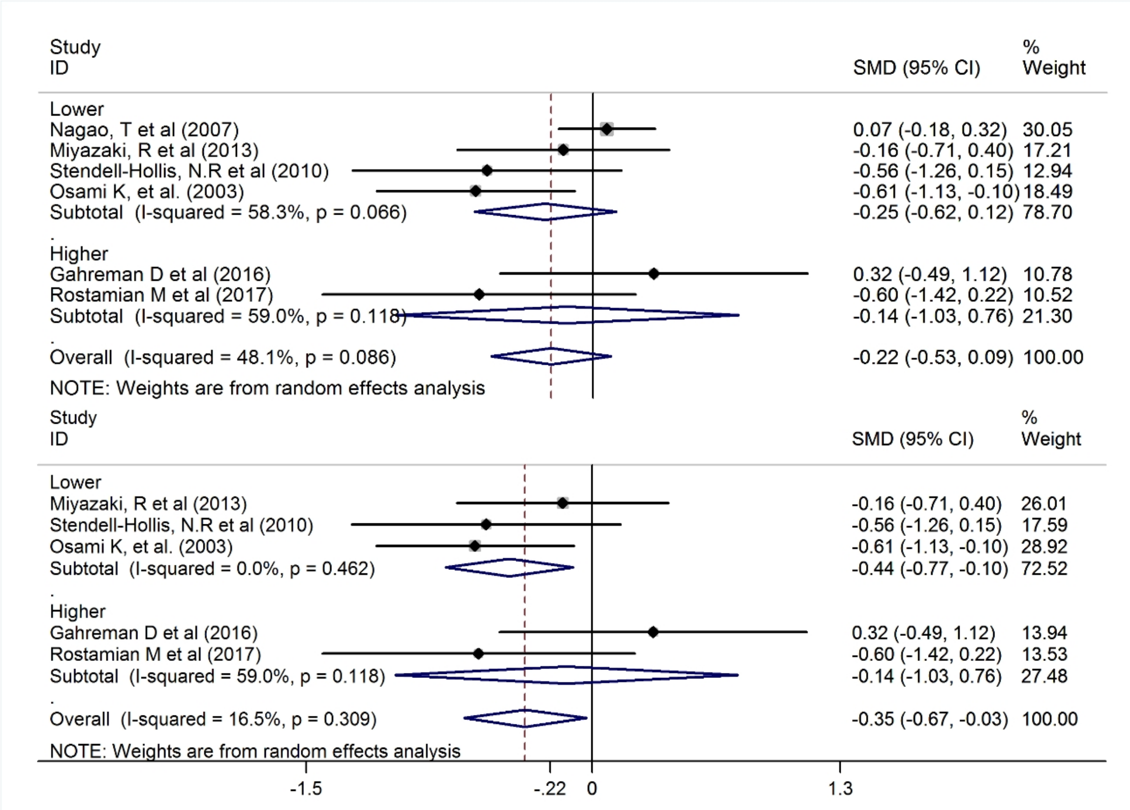


Figure 8 Results of subgroup and sensitivity analysis from difference dose EGCG evaluating the effect of GTE combined with exercise on TC levels (mmol/L). Sizes of data markers indicate the weight of each study in the analysis. (Lower subgroup = lower dose EGCG; Higher subgroup = higher dose EGCG)

5-3-2. Effects of GTE on the HDL-C and TG levels

Seven trials were included in the meta-analysis. The trials reported significant changes in the HDL-C levels of the GTE group after intervention; only one reported a significant increase in the GTE and placebo groups. However, our meta-analysis found no significant increase in the HDL-C level in the GTE combined with physical activity group in comparison to the placebo group (SMD: -0.089; 95%CI: -0.384 to 0.205; I^2=55.6%; p=0.552). According to Egger's test, there was no publication bias (p=0.16). A subgroup analysis revealed that higher-dose GTE was associated with a significant decrease in the HDL-C level in comparison to placebo (SMD:-0.743; 95%CI:-1.331 to -0.154; I^2=0%; p=0.013) (Figure 9). A subgroup and sensitivity analysis failed to show significant differences in the HDL-C level between the plan and daily groups (SMD: -0.177; 95% CI: -0.448 to 0.095; I^2=33.3%; p=0.202).

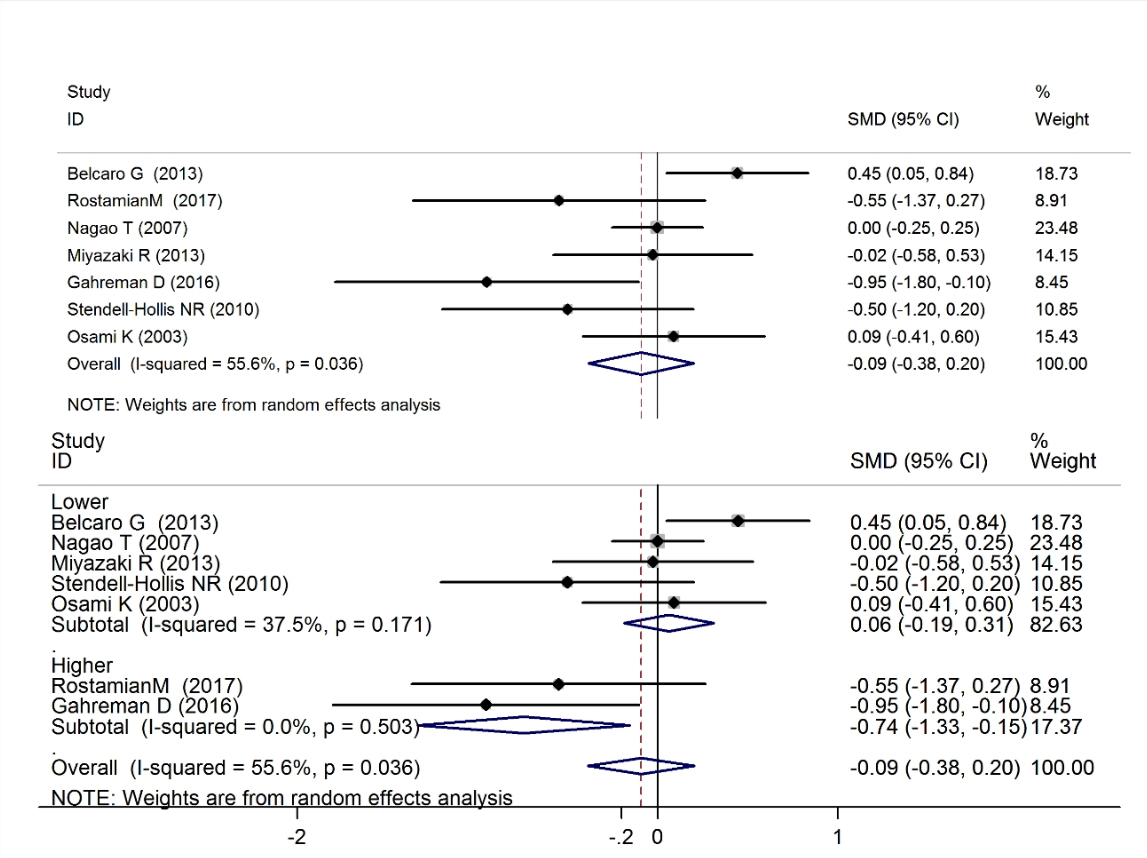


Figure 9 Results of GTE combined with physical activity, subgroup and sensitivity analysis from difference dose EGCG evaluating the effect of GTE combined with exercise on HDL-C levels (mmol/L). Sizes of data markers indicate the weight of each study in the analysis. (Lower subgroup = lower dose EGCG; Higher subgroup = higher dose EGCG)

Three trials reported a significant decrease in TG after intervention in the GTE group, while two showed a significant decrease with the GTE group and placebo group. Our meta-analysis found no significant decrease in the TG level in the GTE combined with physical activity group in comparison to the placebo group (SMD: 0.074; 95 % CI: -0.168 to 0.316; I^2=36.8%; p=0.547). According to Egger's test, there was no publication bias. Our meta-analysis found no significant decrease in the TG level in the GTE combined with physical activity group in comparison to the placebo group (SMD: 0.074; 95 % CI: -0.168 to 0.316; I^2=36.8%; p=0.547). According to Egger's test, there was no publication bias (p=0.593). A subgroup analysis revealed that the TG level of subjects who received higher-dose GTE was not significantly decreased in comparison to placebo nor was any significant difference in the TG level noted between the exercise plan group and the daily activity group. We did not performa sensitivity analysis, even though the subgroup analysis showed heterogeneity in the higher-dose EGCG group, because only two trials included a higher dose of GTE. A subgroup and sensitivity analysis failed to show a significant difference in the TG level between exercise group and daily activity groups (SMD: 0.044; 95 % CI: -0.378 to 0.466; I^2=47.3%; p=0.838).

5-4. Discussion

A total of seven RCTs were included in this meta-analysis, which found no significant differences in the serum HDL-C, LDL-C, and TG levels between the GTE combined with physical activity and the placebo groups. However, subgroup and sensitivity analyses revealed that the TC level was significant decreased in the lower-dose EGCG subgroup. The findings of the present meta-analysis contradict those of a previous meta-analysis, which revealed the beneficial effects of GTE on the lipid and lipoprotein profile (Zheng, et al. 2011). In contrast to the previous review, our meta-analysis also assessed the effects of physical activity on the serum lipids. The studies evaluated here would have been different; thus, there might have been discrepancies between these reviews regarding the findings concerning the beneficial effects of GTE on the lipid and lipoprotein profile (Onakpoya, et al. 2014). However, we did note some similarities in the lipid profiles of the subjects of our review and the subjects of the previous meta-analysis.

Protecting human LDL-C levels against oxidative attack is an important action of tea polyphenols; however, the mechanisms through which LDL-C oxidation is inhibited are unclear (Senanayake 2013). GTE affects the human body via two major mechanisms: (1) tea polyphenols decrease the digestion and absorption of macronutrients in the gastrointestinal tract; and (2) tea polyphenols inhibit the anabolism and stimulate the catabolism of skeletal muscle, liver, and adipose tissues (Yang, et al. 2016). Studies have revealed that CVD is associated with oxidative stress induced lipid damage. Tea polyphenols therefore reduce this damage and enhance the endogenous defense system (Gadkari, et al. 2015). However, we found no significant decrease in the LDL-C and TC levels in our review. Although the previous meta-analysis found that GTE did indeed reduce these levels (Kim, et al. 2011). In comparison to the previous study, we considered physical activity as an important factor in our review. Increasing physical activity is effective for preventing CVD. However, in the present study, the combination of physical activity and GTE showed no significant effect. Of note, while we found no significant decrease in the LDL-C levels of the subjects in our meta-analysis. We did find a significant decrease in the TC levels in a sensitivity analysis. A study of tea polyphenols showed that EGCG, EGC, ECG, and EC are the main of tea catechins, along with their gallate esters (gallocatechingallate, gallocatechin, catechingallate, catechins). A systematic review reported that the dose of EGCG in most studies exceeded 200 mg. An observational study review found that people who drank 1-3 cups of green tea enjoyed a reduced risk of CVD, and that an increase in green tea consumption by 3 cups daily was associated with a reduced risk of cardiac death (Zhang, et al. 2015). Koutelidakis showed that a lower dose of tea catechins failed to improve the levels of LDL-C and TC levels (Koutelidakis, et al. 2014). In comparison to those previous studies, the studies included in the present meta-analysis might have involved a lower dose of EGCG; indeed, the lowest dose of EGCG was 39mg, and the highest was 375mg. This may explain the lack of any significant findings in our review.

Because of the limited number of studies available, we included all of the eligible human studies regardless of the subjects' health. This resulted in the inclusion of patients with metabolic syndrome, obese subjects, and breast cancer survivors in our review. The LDL-C levels varied markedly among our populations, which featured postmenopausal women, patients with hypercholesterolemia, and older subjects. The cholesterol concentrations also varied according to age and body mass index, which might be why our review revealed no significant finding (Hall G 2002). Two RCT studies by Samavat et al. (Samavat, et al. 2016) and Wu et al. (Wu, et al. 2012) showing that green tea catechins were able to reduce the level of LDL-C in postmenopausal women (high-dose EGCG[400-843mg/day]). This might have been a major confounding factor in our meta-analysis.

While several meta-analyses have reported significant improvement in the lipid and lipoprotein content with physical activity (Durstine, et al. 2001, Kelley, et al. 2006, Zhang, et al. 2013), few studies have shown significant changes in the TC and LDL-C levels specifically (Thompson, et al. 2003). Furthermore, these beneficial effects were typically noted in studies including diet intervention or obese participants (Durstine, et al. 2001). A previous meta-analysis also reported non-significant decreases in the TC and LDL-C levels, although major cardio-protective improvements in the LDL-C levels subfractions may have occurred (Kelley, et al. 2006). In our review, the sensitivity analysis revealed that the TC level was significantly decreased in association with daily activity. This may be due to the methods in studies that used physical activity combined with GTE. Studies have shown that many confounding factors can influence the effects of interventions targeting TC and LDL-C levels, including body characteristics, energy expenditure, food supplements, health status, and lifestyle. Consequently, the results obtained in our analysis might be because the eligible studies all included population with differences in health status, age, and degree of physical activity.

Aerobic exercise has been shown able to improve the TG and HDL-C levels, although a less-marked response is observed for LDL-C and TC levels (Ghahramanloo, et al. 2009, Popovic, et al. 2010). However, we found no significant differences in the HDL-C and TG levels between the GTE combined with physical activity, and exercise subgroups and the daily activity group. A meta-analysis reported that a large amount of high-intensity exercise exerted a beneficial effect on the HDL-C and TG levels (including high-amount and high intensity, low-amount and high intensity or low-amount and moderate intensity exercise) (Kraus WE 2002). Furthermore, Kodama et al (Kodama, et al. 2007) reported that regular aerobic exercise increased the HDL-C levels, with greater improvement seen with a longer duration of exercise. In our included studies, more than half articles used regular exercise. However, three of the RCTs in our meta-analysis included overweight or obese subjects, and caloric restriction was not reported. A previous study reported that regular exercise has beneficial effects on the lipoprotein profile, and that a higher amount of exercise has a much greater beneficial effect on the serum lipid content than a lower amount of exercise (Mora S 2007). In addition, there was difference health statuses of the individuals included in our review. This may explain why we failed to observe a significant improvement in the TG and HDL-C levels in the exercise subgroups. Exercise also reduces the TG levels and increases the HDL-C level. However, there no significant differences were noted in the TG levels of the exercise subgroup in our review. Endurance exercise and acute exercise studies have shown that aerobic exercise combined with resistance training was effective in reducing the TG level (Couillard C 2001, Ho, et al. 2011). A study of the effects of the amount and intensity of exercise on the plasma lipoprotein levels reported that the TG level was significantly changed, in response to high-amount-high-intensity, low-amount-high-intensity, and low-amount-moderate-intensity exercise. In contrast, although a trend toward a reduction in the TG level was found, exercise combined with GTE had no significant effect on the TG level.

A few studies have reported significant effects of GTE on the levels of HDL-C and TG, Vinson (Joe A Vinson 1998) showed that GTE was able to increase the HDL-C level in normal and high-cholesterol-diet hamsters. Guo et al. further confirmed that GTE improved the HDL-C and TG levels in high-cholesterol-diet mice (Guo, et al. 2016). However, meta-analyses of 7 trials failed to show significant effect on the HDL-C or TG levels. A systematic meta-analysis showed that green tea had no significant differences in the HDL-C and TG levels in humans (Kim, et al. 2011). Similarly, another study reported that GTE for 3 weeks had no effects on serum lipid markers, such as HDL-C and TG levels (Eichenberger, et al. 2010). Our study also showed no significant changes in the HDL-C and TG levels following GTE treatment, and in subgroup and sensitivity analysis. Furthermore, Bogdanski et al (Bogdanski, et al. 2012) and Hsu et al (Hsu, et al. 2008) showed that a higher dose of GTE increased the levels of HDL-C and TG levels in their RCTs. Few studies have confirmed the beneficial effects of GTE on the HDL-C and TG levels. More animals and/or human studies are needed to evaluate the relationship between with the GTE or GTE in combination with physical activity and HDL-C and/or TG levels.

Strengths and limitations

In comparison to the previous meta-analysis, the strength of this review is mainly that this is the first systematic review and meta-analysis focusing on the effects of GTE combined with physical activity on the lipid and lipoprotein content in humans. Furthermore, our findings contradict the results of the effects of GTE that were reported in previous reviews. However, there are several limitations that should be acknowledged. First, the eligible studies included data on GTE and physical activity from only a few RCTs, which restricted the accurate assessment of the type-response relationship between GTE combined with physical activity and the serum lipid content in humans. Second, due to the limitations of the included studies, we were unable to restrict the characteristics of the subjects enrolled. This represents an important confounding factor that affected the results or meta-analysis. Third, only one study reported the energy expenditure of its subjects. Thus we cannot evaluate the intensity of exercise, which is known to be associated with the degree of improvement in the serum lipid level. Finally, a few studies only used a pedometer to assess physical activity, and they did not report the detailed results of the daily activity of their subjects. These limitations might have undercut the strengths of this review.

In conclusion, the findings from previous studies collectively suggest that GTE combined with physical activity does not seem to be associated with the lipids and lipoprotein content of humans. However, due to the limited number of eligible studies, we could not obtain a clear result. These complex issues should be explored in better designed RCTs in the future.

6. Hypothesis

The effect of the combination of GTE and brisk walking on lipid profile, body shape, fasting glucose and physical fitness function in overweight and obese men, does not appear to have been examined. Due to many confounding factors can influence the effects of interventions targeting these outcomes, including body characteristics, daily dosages of GTE, energy expenditure, health status, lifestyle and degree of physical activity. Therefore, in this thesis, we decided to examine three different hypotheses in one intervention study.

The first hypothesis of this thesis is that combination of brisk walking and GTE might improve the lipid profile and liver function in overweight and obese men. These beneficial effects are due to GTE was able to inhibit and reduce the cholesterol absorption and synthesis. In addition, exercise has a positive effect on reverse cholesterol transport, and then improves the lipid profile. The second hypothesis is that GTE combined with brisk walking might improve FG levels and body shape in inactive overweight and obese men under uncontrolled dietary condition. These beneficial effects are due to GTE was able to inhibit the carbohydrate digestive enzyme activity and increase the translocation of glucose transporters. And brisk walking was able to increase the caloric expenditure. The third hypothesis is that GTE combined with brisk walking might improve the aerobic capacity and physical fitness function in participants, and GTE group might have more effective than brisk walking group. These beneficial effects are due to aerobic exercise was able to improve the aerobic capacity and physical fitness function. In addition, GTE is able to increase fatty acid oxidation in skeletal muscle, and improve the endurance capacity.

Chapter 2. Effects of green tea extract combined with brisk walking on lipid profiles and the liver function in overweight and obese men: A randomized, double-blinded, placebo-control trial

1. Introduction

The prevalence of overweight and obesity has increased dramatically over the last four decades. About 1.9 billion were overweight and 650 million adults were obese in 2016 according to the world health organization (WHO) (Jaacks, et al. 2019). According to the Chinese General Social Survey (CGSS), about 31% of the population was overweight or obese (Zhou 2019) (overweight: body mass index [BMI] ≥ 24 kg/m^2; obesity: BMI ≥ 28 kg/m^2). Obesity is an important risk factor for hypertension, type 2 diabetes mellitus, cardiovascular disease (CVD), insulin resistance, metabolic syndrome, and dyslipidemia, and is also associated with an increased mortality rate and disability (Bastien, et al. 2014). Studies (Oliveros, et al. 2014, Piepoli, et al. 2016) have reported that obesity is associated with high levels of low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and triglyceride (TG), and low levels of high-density lipoprotein cholesterol (HDL-C) as important risk factors for the development of dyslipidemia, hyperlipidemia, and atherosclerosis. As physical activity and GTE have been shown to be associated with the management of obesity and lipids cholesterol, there is great interest in exercise and GTE modifications to help improve the body composition and treat chronic diseases.

Increased physical activity is an important component of therapy for obesity management. Brisk walking as a simple, economic, and safe form of exercise is the most popular moderate-intensity aerobic physical activity for both men and women, especially for most middle-aged and/or overweight and obese individuals (Siegel, et al. 1995). A previous study showed that moderate exercise (energy expenditure 1200 to

2200 kcal/week of brisk walking or jogging) effectively elevate HDL-C levels from 2 to 8 mg/dl and lower TG levels by 5 to 38 mg/dl (Durstine, et al. 2001). In addition, a met-analysis review (Kelley, et al. 2006) showed that aerobic exercise increases the HDL-C levels and reduces the TG levels in patients with CVD. However, Cai et al. (Cai, et al. 2016) conversely reported that a meta-analysis of nine studies found that aerobic exercise (seven studies involved a walking program) only reduced the TG levels in overweight or obese adults, with a significant changes in the HDL-C level noted only in female subgroup.

Green tea is a natural supplement, and its beneficial effects for promoting health have been intensively investigated in the past decade (Binns, et al. 2008, Isemura, et al. 2015). Green tea is rich in catechins, and epigallocatechin-3-gallate (EGCG) is the most abundant and pharmacologically active of these catechins (Chen, et al. 2016). Animal studies have shown that green tea or green tea extract (GTE) effectively regulates LDL-C oxidation and reduces the blood levels of cholesterol in rats/mice fed a high-fat diet. The main mechanism underlying the effect of green tea or GTE on blood lipids is the inhibition of dietary lipid absorption and reduction in cholesterol synthesis (Yang, et al. 2016). Recently, meta-analysis and systematic review studies (Kim, et al. 2011, Onakpoya, et al. 2014) reported that green tea or GTE has a significant effect on the LDL-C and TC levels in humans. However, these effects on the lipid profiles of humans are inconsistent and completely opposite results have been obtained in some studies, focusing on green tea or GTE in combination with exercise Gahreman et al. (Gahreman, et al. 2016). Furthermore, Maki et al. (Maki, et al. 2009) reported that 12 weeks of moderate exercise combined with green tea catechin had no effect on the LDL-C and TC levels, although it did affect the TG levels. In addition, studies focus on the liver injury caused by tea catechins (Wolfram 2007), but catechins have a potential positive effect on the liver function (Cheng, et al. 2018).

The knowledge of a potential beneficial effects of GTE combined with brisk walking on the lipid profiles and liver function in inactive overweight and obese adults' men is limited, especially those with under uncontrolled dietary condition (Song, et al. 2017). We hypothesized that GTE combined with brisk walking might improve the lipid profile and liver function in overweight and obese men. Therefore, the aim of this study were (1) to examine the effects of GTE combined with brisk walking on change in lipid profile after 12 weeks and 4 weeks follow-up in inactive overweight and obese men. (2) to investigate the effects of combination of GTE and brisk walking on change in liver function after 12-week and 4 weeks follow-up in overweight and obese men.

2. Materials and Methods

2-1. Study design

This study is a randomized, double-blind, placebo-controlled trial. This study was approved by the Luohe Central Hospital of Clinical Research Ethics Committee (No. 2018-03-015-E01) and has also been registered as a clinical trial (Chinese Clinical Trials Registry, ChiCTR1900025134).

2-2. Participants

Twenty-four overweight and obese men were included in the study. According to the physical characteristics of Asian, the optimal BMI cut-off value is 24 kg/m^2 for men (Zeng, et al. 2014). Those who met the following inclusion criteria were then included: male; between 25 and 59 years of age, BMI between 24 and 32, none were regular exercise training, no participation in any clinical program within the previous 3 months. The exclusion criteria were as follows: regularly consume ＞2 cups of green tea/day, diabetic, history of medication usage in the last 4 weeks, history of serious cardiovascular disease, diagnosed with a mental illness or liver, renal or nerve disease.

2-3. Sample size and randomization

Twenty-four participants were included in this study. The sample size was determined from the sample size recommended in a clinical trial (total 20 participants, assuming a dropout rate of 20%) (Whitehead, et al. 2016). Twenty-four participants were randomly divided into two groups: a GTE and placebo group. Randomization was performed by a randomized digital table sequence with stratified randomization accounting for the potential bias factor of BMI (<27 and ⩾27 kg/m^2). The first author screened and recruited participants and a research assistant preformed the randomization and guarded the results. The GTE and placebo supplement, with A indicating the placebo supplement and B indicating the GTE supplement (determined by a coin toss). The alphabet was marked from the GTE Company, which was managed by another study assistant.

2-4. Procedures

The walking program consisted of four 60-min sessions per week, each including a 5 min warm-up and 5 min cool-down period. This walking program was performed under the supervision of the first author and a research assistant. Due to all subjects being physically inactive overweight or obese men, for the first 3 weeks (initiation phase), we set the target heart rate (HR) to 50%- 65% of the maximum HR for all participants and then gradually increased the intensity (65%-80%) (Murtagh EM, et al. 2002). The maximum HR was calculated using the equation HR_{max} = [220－age]. All participants were fitted with a heart rate monitor (FS1, Polar, Finland). The participants were also fitted with a pedometer (Power walker, EX-510; Yamax, Tokyo, Japan), which recorded the step counts during the exercise period. In the intervention period, all participants were asked to consume two GTE or placebo tablets daily (one after breakfast and one after dinner) and to drink a cup of water.

2-5. supplement and diet

GTE (EGCG) and placebo were purchased from Damingtang Company (Hangzhou, China). Each GTE tablet contained 150 mg of EGCG (95% pure), isomaltitol, and microcrystalline cellulose (MC), and each placebo tablet contained neutral ingredients, such as corn starch, MC and isomaltitol. We did not manage the diet of the participants.

2-6. Biochemical parameters

All participants visited the hospital 3 times: at baseline, at 12 weeks after the start, and at 16 weeks after the start (for the 4-week follow-up). Venous blood samples (5 mL) were obtained from all participants after fasting for 8-10 h (8:30-10:00 AM). Blood samples were analyzed for TC (mmol/L), LDL-C (mmol/L), HDL-C (mmol/L) and TG (mmol/L) as well as serum aminotransferases (alanine transaminase, [ALT], aspartate aminotransferase [AST], γ -glutamyl transpeptadase [GGT], total bilirubin [TBIL]). All parameters were measure at the center laboratory, Luohe Central of Hospital.

2-7. Statistical analysis

All statistical analyses were performed using SPSS 20.0 software program (IBM SPSS Statistics, Armonk, USA). The intention-to-treat (ITT) efficacy analysis was used in this study. Results are reported as the mean ±standard deviation (SD) for continuous variables unless otherwise stated. The baseline differences between groups were analyzed on all demographics using independent sample *t*-tests for continuous variables. The Shapiro-Wilk normality test was used to test data normality. If the data were not normality distributed, a Wilcoxon's test was used within the groups. To examine the changes between the groups after the intervention, we used analysis of co-variance (ANCOVA) to analyze the data. After observing the normality, a parametric analysis was performed using a repeated measure analysis of variance (2 groups by 3 moments [baseline, post-test and follow-up]). For all comparisons, a P value of < 0.05 was considered significant.

3 Results

3-1. Participants and baseline characteristics

Twenty-four subjects were recruited from among 39 potential candidates between September 2018 and October 2018. All participants were randomly assigned to the GTE group or placebo control group. Two participants (one each in the GTE group and placebo control group) dropped out of the study during the intervention period, due to gastrointestinal discomfort caused by the GTE or placebo. Another two participants (one each in the GTE group and placebo control group) dropped out of the study during the follow-up period, because of their jobs.

An analysis of the baseline characteristics of participants showed no significant differences between the groups in the age, body weight, BMI, systolic blood pressure, or diastolic blood pressure (Table 3). There were also no significant differences in the LDL-C, HDL-C, TC, TG, ALT, AST, TBIL, or GGT levels between the groups at baseline.

Table 3 Subject characteristics at baseline

Variable	GTE group (n= 12)	Placebo group (n= 12)
Age (years)	42.5±9.82	37.2±7.2
Body weight (kg)	83.0±9.37	82.3±8.46
Body mass index (BMI)	28.4±2.24	27.7±2.26
LDL-C (mmol/L)	2.91±0.886	2.82±0.839
HDL-C (mmol/L)	1.43±0.252	1.33±0.123
TC (mmol/L)	4.85±1.069	4.78±1.105
TG (mmol/L)	1.64±1.026	2.03±1.100
ALT (U/L)	35.2±15.52	45.8±22.67
AST (U/L)	23.0±6.38	26.6±9.22
TBIL (U/L)	18.9±5.24	17.7±4.38
GGT (U/L)	43.5±31.22	54.3±47.48

3-2. The between-group ANCOVA

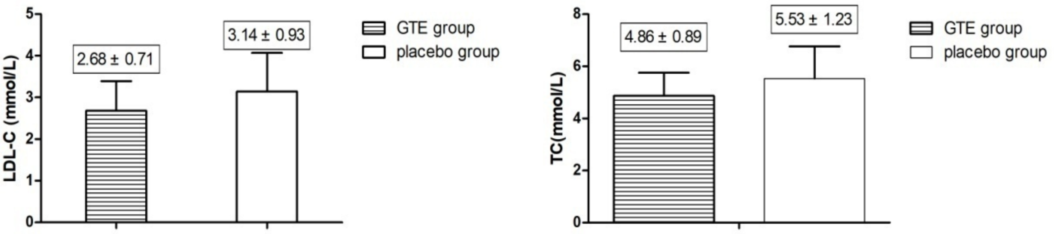
The changes between groups were analyzed by an ANCOVA, with the pre-intervention levels as covariates and post-intervention levels as dependent variables. As shown in Table 4, there was a significant difference in the LDL-C levels between the GTE group and placebo group ($P < 0.05$). A comparison between the groups also showed a significant change in the TC levels ($P < 0.05$) (Figure 10). There were also no significant differences in the HDL-C and TG levels and the liver function (ALT, AST and TBIL levels) between the GTE group and placebo group. The GGT parameters did not conform to a normal distribution (Shapiro-Wilk normality test: P = 0.000), and therefore, the results of Wilcoxon's test showed that there were no significant differences either between or within the groups.

Table 4 Blood lipid profiles and liver function in ANCOVA after 12 weeks intervention

	GTE group (n= 12)				Placebo group (n= 12)					
	Unadjusted		Adjusted		Unadjusted		Adjusted			
	Mean	SD	Mean	SE	Mean	SD	Mean	SE	F	*P*
LDL-C(mmol/L)	2.68	0.708	2.64	0.11	3.14	0.928	3.18	0.11	12.651	0.002*
HDL-C(mmol/L)	1.32	0.241	1.28	0.04	1.32	0.188	1.36	0.04	2.507	0.128
TC (mmol/L)	4.86	0.894	4.84	0.16	5.53	1.235	5.56	0.16	10.337	0.004*
TG (mmol/L)	1.40	0.527	1.52	0.15	1.89	0.992	1.77	0.15	1.512	0.233
ALT (U/L)	30.8	15.97	33.6	3.68	42.7	15.56	39.9	3.68	1.433	0.245
AST (U/L)	18.7	5.65	19.6	1.29	23.7	6.26	22.7	1.29	2.717	0.114
TBIL (U/L)	13.9	5.22	13.5	0.98	12.5	3.35	12.8	0.98	0.271	0.608

Note: pre-intervention levels as covariates and post-intervention levels as dependent variables. Unadjusted: Values are expressed as mean ±standard deviation (SD). Adjusted: Values are expressed as mean ±standard error (SE).* Significant difference ($p < 0.05$).

A



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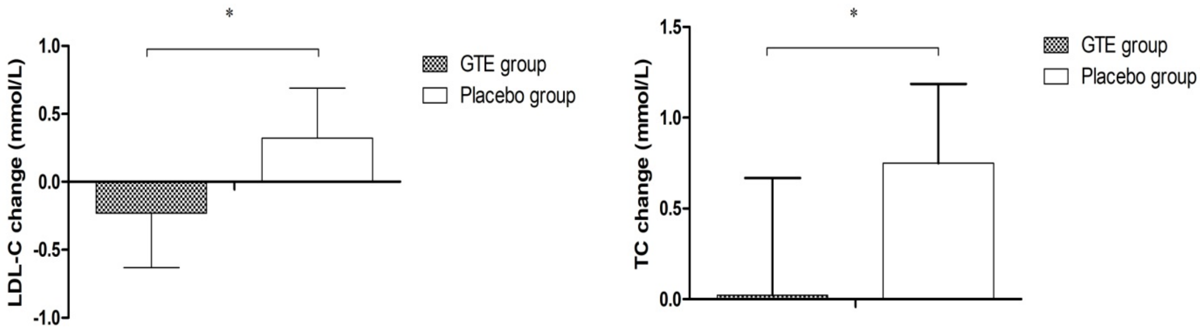


Note: Values are adjusted for baseline value. A: after 12 Week's intervention; B: The difference in Pre-Post between groups. LDL-C, low density lipoprotein cholesterol; TC, total cholesterol. * Significant difference ($p < 0.05$).

Figure 10 Changes in the LDL-C and TC levels after 12 weeks intervention

3-3. Repeat assessments

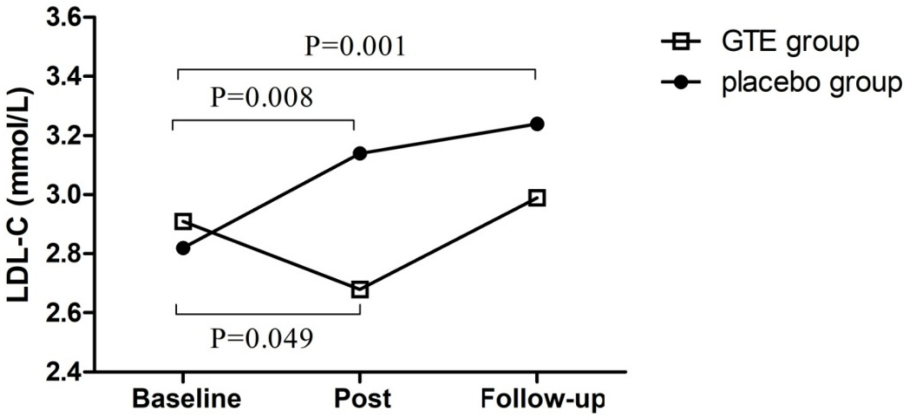
Table 5 shows the lipid profiles and the liver function parameters with three-fold measurement for the two groups. Across both groups, significant time main effects were found in the LDL-C, HDL-C, TC, and TBIL levels. The placebo group showed increased LDL-C (*P* = 0.024) and TC (*P* = 0.000) levels and decreased TBIL (*P* = 0.000) levels. The GTE group, showed decreased LDL-C levels after intervention, and decreased HDL-C (*P* = 0.008) levels. A significant group main effect was found for AST levels (*P* = 0.024) with the placebo group, and there was a significant difference in the AST levels between the two groups in the follow-up period. A group × time effect was found for TC levels (*P* = 0.013), with the placebo group showing a dramatic increase and the GTE group a slight decrease. A significant group × time effect was also found for the HDL-C levels (*P* = 0.008), with the GTE group showing a slight decrease and the placebo group consistently normal.

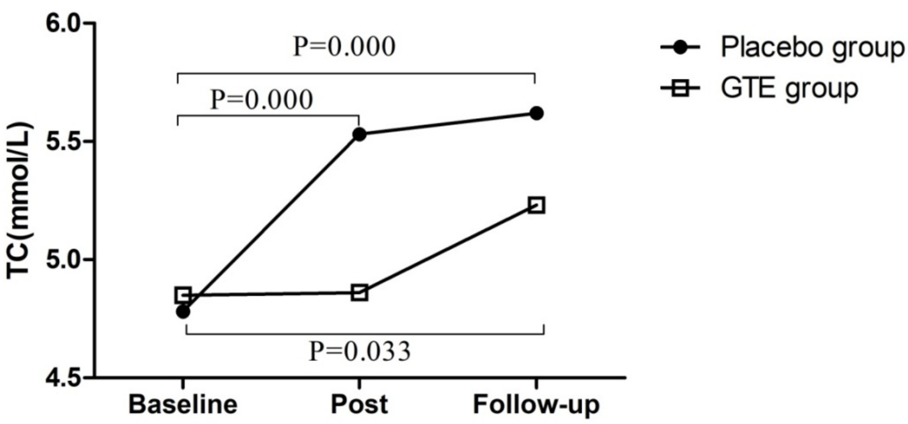
Table 5 Biochemical analysis of the participants during the experimental and follow-up

Variable	GTE group (n= 12)			Placebo group (n= 12)			P-value		
	Pre	Post	Follow-up	Pre	Post	Follow-up	Group	Time	Group ×Time
LDL-C	2.91±0.886	2.68±0.708*	2.99±0.910&	2.82±0.839	3.14±0.928*	3.24±0.753#	0.546	0.024	0.163
HDL-C	1.43±0.252	1.32±0.241*	1.33±0.275#	1.33±0.123	1.32±0.126	1.28±0.116	0.528	0.008	0.006
TG	1.64±1.026	1.40±0.527	1.52±0.497	2.03±1.100	1.89±0.992	1.88±1.106	0.222	0.428	0.910
TC	4.85±1.069	4.86±0.894	5.23±1.190#	4.78±1.105	5.53±1.235*	5.62±0.994#	0.451	0.000	0.013
ALT	35.2±15.52	30.8±15.97*	28.2±15.40	45.8±22.67	42.7±15.56	51.33±38.90	0.054	0.622	0.317
AST	23.0±6.38	18.7±5.65*	17.3±5.68	26.6±9.22	23.7±6.26	27.3±12.56§	0.024	0.124	0.181
TBIL	18.9±5.24	13.9±5.22*	14.4±5.49#	17.7±4.38	12.5±3.35*	10.9±4.07#	0.229	0.000	0.415
GGT	43.5±31.22	34.9±15.13	37.5±19.03	54.3±47.48	50.6±46.39	51.4±46.21	0.368	0.108	0.592

Note: Values are expressed as mean ±SE. *, #, & $p < 0.05$; * *P*-value for within-group comparisons in pre-and-post period; # *P*-value for within-group comparisons in post and follow-up; & *P*-value for within-group comparisons in pre and follow-up. § *P*-value for between group comparisons in follow-up period. TC (mmol/L); LDL-C (mmol/L); HDL-C (mmol/L); TG (mmol/L); ALT(U/L); AST(U/L); TBIL(umol/L); GGT(U/L).

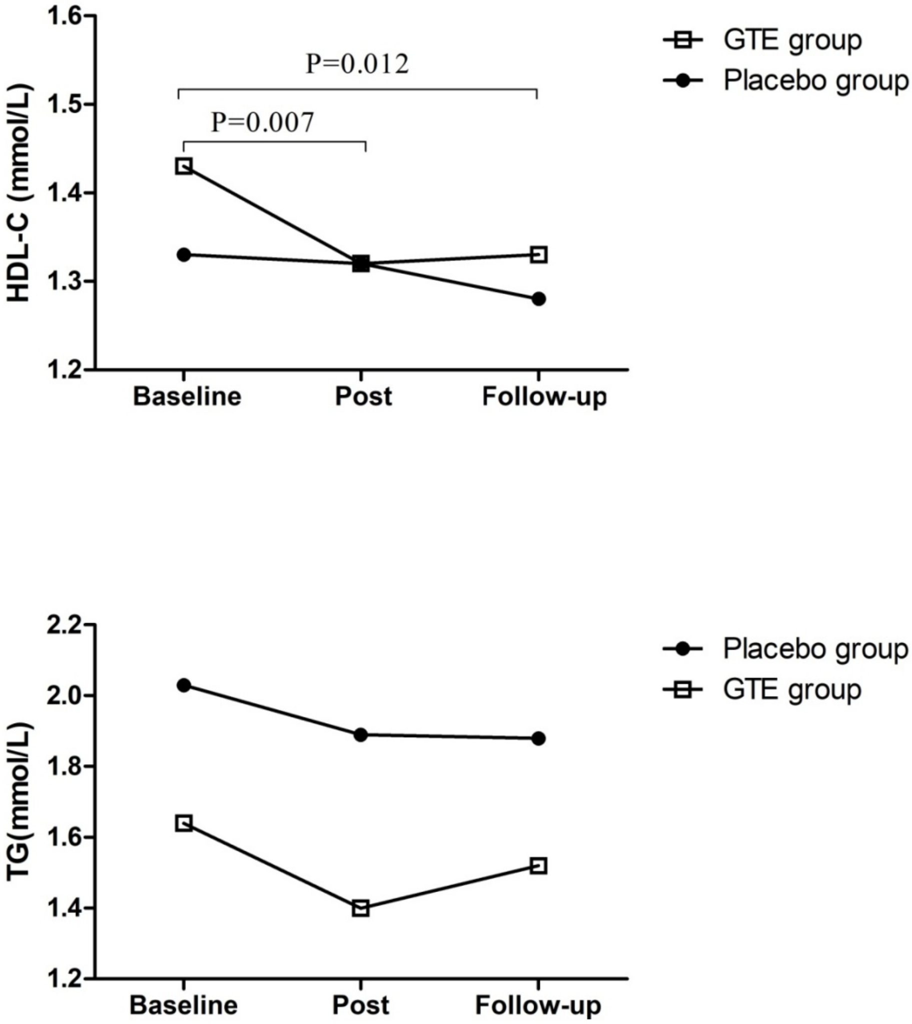
As shown in Table 5, there was a significant change in the LDL-C levels after 12 weeks' intervention for the GTE group ($P < 0.05$). There was also a significant reduction in the HDL-C levels in the GTE group ($P < 0.05$), but no significant difference was observed in the HDL-C levels for the placebo group. There was also no significant change in the TG levels for either group after 12 weeks' intervention (Figure 12). There was a significant increase in the LDL-C and TC levels in the GTE group after the 4-week follow-up period (Figure 11). Liver function tests showed a significant difference in the TBIL levels for the GTE and placebo group baseline and after 12 weeks' intervention. There was a significant change in the AST levels for the GTE group ($P < 0.05$), but no significant difference was found for the placebo group ($P = 0.162$) (Figure 13). There was no significant difference in the GGT levels for either group after 12 weeks of intervention and at the 4-week follow-up.





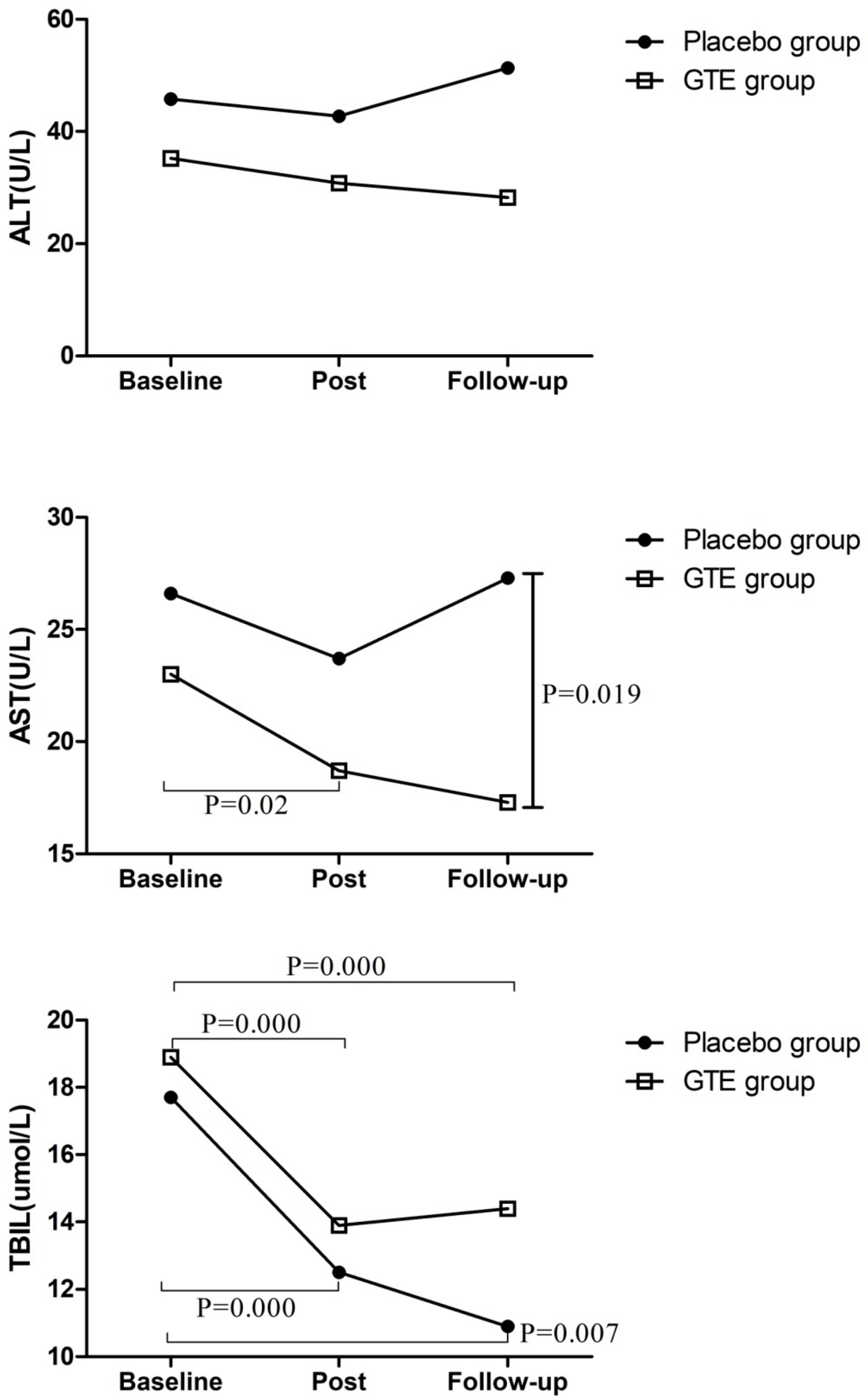
Note: LDL-C, low density lipoprotein cholesterol; TC, total cholesterol.

Figure 11 Effect of GTE combined with brisk walking on the LDL-C and TC levels



Note: HDL-C: high density lipoprotein cholesterol; TG: triglyceride.

Figure 12 Effect of GTE combined with brisk walking on the HDL-C and TG levels



Note: ALT: alanine transaminase; AST: aspartate aminotransferase; TBIL: total bilirubin.

Figure 13 Effect of GTE combined with brisk walking on the ALT, AST, and TBIL levels

4. Discussion

This study was designed to assess the effects of GTE combined with brisk walking on lipid profiles and liver function in inactive overweight and obese men. Compared with the placebo group, ingestion of GTE for 12 weeks significantly reduced the LDL-C levels in overweight and obese men. Worth noting is that there was no significant change in the TC levels in the GTE group even after 12 weeks' intervention; however, EGCG was able to significantly control the TC levels in overweight and obese men, and we observed a significant increase in the GTE group after 4 weeks follow-up. Recently, studies (Cicero, et al. 2017, Onakpoya, et al. 2014) reported that green tea results in a significant reduction in TC and LDL-C levels. Furthermore, in animal studies (Murase T 2002, Richard, et al. 2009), authors have reported that green tea or GTE significantly reduced LDL-C and TC levels in rats/mice. The mechanism underlying the reduction in plasma cholesterol levels by GTE might involve EGCG preventing the absorption of lipids and inhibiting digestive enzymes, with additional effects on the intestinal microbiota (Suzuki, et al. 2016). The present findings are largely in agreement with those of previous studies, although there are some differences.

The discrepant results between the present study and the conclusion of the previous meta-analysis may be due to the following: first, as the table 3 shown, GTE have a positive effect on improvement the TC levels. The present study used a dose of only 300mg EGCG/day (Dekant, et al. 2017); however, many, but not all, previous studies demonstrating significant changes in LDL cholesterol and TC levels used higher doses of GTE (EGCG). Samavat (Samavat, et al. 2016) reported a significant reduction in LDL-C and TC levels in postmenopausal women after 1 year of consuming a supplement with green tea catechins (1315 mg/day) compared to the baseline and placebo group. In addition, a 2-month randomized control trial of green tea (EGCG: 400mg/day and 800mg/day) found a significant change in the TC and LDL-C levels in healthy postmenopausal women (Brown, et al. 2011).

Another important confounding factor may be the diet. Previous study (Li, et al. 2017) noted the over-consumption of high-fat and deep-fried foods in the Chinese dietary pattern over the past few decades. Data from animal studies (Huang, et al. 2018, Wang, et al. 2018) have indicated that a high-fat diet combined with GTE results in a significant change in the LDL-C and TC levels in mice/rats. In another study, Li et al. (Li, et al. 2004) reported that meat was consumed more frequently in the winter than in the summer for a large number of Chinese individuals, and the summer months showed a more balanced dietary pattern than the winter months (Zang, et al. 2017). Our study was started in November and ended the following February, which is the winter period in north China. These findings indicate that a high-fat diet is an important confounding factor in the intervention period, and the season was also a confounding factor.

Although a previous study (Cai, et al. 2016) found that brisk walking significantly altered the HDL-C and TG levels in humans, we noted no significant changes in the HDL-C and TG levels in the placebo group in our present study, and while a significant decrease in the HDL-C levels was noted in the GTE group, there were no significant differences in the TG levels. The reason might be due to all participants were inactive overweight and obese men and the intensity of brisk walking. Durstine et al. (Durstine, et al. 2001) reported a significant increase in the HDL-C levels and a significant reduction in the TG levels, when subjects achieved 24-32 km per week of brisk walking or jogging and elicit between 1200 to 2200 kcal/wk. In the present study, although we set the target heart rate to 50% - 80% in the two phases during the intervention period, the participants were not achieved. Study by Andersen et al. (Andersen, et al. 2013) showed that dietary components have a significant effect on the HDL-C function. The over-consumption of cereal, meat, and poultry in Chinese dietary patterns might be the other reason (Song, et al. 2017). The significant reduction in the HDL-C levels in the GTE group might be due to the mechanism of cholesterol metabolism; a recent animal study (Liao, et al. 2016) found a significant reduction in the HDL-C levels after feeding green tea polyphenols to high-fat-diet mice for several weeks. The results of the present study are in agreement with those of that animal study. This outcome might be due to HDL-C playing a role in cholesterol metabolism. Another study (Cavallini, et al. 2011) showed that HDL-C level is positively correlated with the *Bifidobacteria* populations in the gut. Furthermore, an animal study (Liao, et al. 2016) found that EGCG significantly increased the number of *Bifidobacteria* in the gut and reduced the serum cholesterol level.

Finally, significant changes in AST levels but only a downward trend in ALT levels was noted in the GTE group. These findings for ALT levels in the present study demonstrate that GTE has a beneficial effect on the liver function. The effect of GTE on the liver function in this study agrees with the results of a recent meta-analysis of four trials, which showed a significant effect on the ALT and AST levels in cases of non-alcoholic fatty liver disease (NAFLD) (Mansour-Ghanaei, et al. 2018). A daily consumption of 300mg EGCG combined with brisk walking for 12-week positively influenced the liver function biomarkers in overweight and obese men in the present study. We also found that a positive effect on the serum LDL-C and TC levels in overweight and obese adult men. However, there was a negative effect on the HDL-C levels in the GTE group. Further studies on the effects of GTE combined with brisk walking on the HDL-C levels in overweight and obese men should be conducted.

Several limitations associated with the present study warrant mention. First, the sample size in this study was relatively small. Second, a relatively low dose GTE was used. Third, we did not control the diet in the present study. A multi-arm and larger-scale trial should be conducted in order to confirm the present study's results.

In conclusion, the results of this study provide evidence that GTE combined with brisk walking in inactive overweight and obese men for 12 weeks did not reduce the TG levels within the groups. However, this study confirmed that GTE combined with brisk walking was able to significantly control LDL-C and TC levels compared with the placebo group. In addition, our study shows that GTE combined with brisk walking is sufficient for improving the liver function than exercise alone. There was a downward trend in the lipid profiles in the follow-up period in both groups.

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Chapter 3. Effects of brisk walking combined with green tea extract on fasting glucose and body shape in overweight and obese men: A randomized, double-blinded, placebo-control trial

1. Introduction

Over the last three to four decades, the proportion of individuals with obesity has increased dramatically worldwide. Excess weight is a well-recognized risk factor for several common chronic conditions, including dyslipidemia, atherosclerosis, type 2 diabetes, metabolic syndrome, and other health problems (Kirwan, et al. 2017). Studies have also shown that obesity is associated with high glucose levels and type 2 diabetes (Rao, et al. 2019). Exercise or physical activity was most frequently chosen as methods to improve fasting glucose (FG) levels or manage body shape (Lee, et al. 2008). Walking has been described as a near perfect ‘‘exercise’’ and has been recommended by health organizations worldwide (Hardman, et al. 1998). Brisk walking is one of the most popular moderate-intensity aerobic physical activities for both men and women, especially for middle-aged and/or overweight and obese individuals (Pillay, et al. 2014). Exercise or physical activity was most frequently chosen as methods to improve FG levels or manage body weight (Lee, et al. 2008).

Green tea is a natural supplement. The ingestion of GTE (270 - 1200 mg/day) may be associated with loss of body weight and fat (Suzuki, et al. 2016, Wang, et al. 2014). The predominant constituents of green tea are polyphenols, and most of which are catechins. Epigallocatechin-3-gallate (EGCG) is the major component of tea catechins, and the most pharmacologically active (Feng 2006). A previous study (Sae-tan, et al. 2011) on green tea and /or green tea extract showed numerous potential benefits for managing obesity and improving fasting glucose levels. Study by Sylow et al. (Sylow, et al. 2017) also reported that exercise is a cornerstone to therapy the metabolic diseases such as type 2 diabetes. In addition, Martin et al. (Martin, et al. 2016) reported that GTE combined with exercise effectively regulates glucose metabolize and reduces the skeletal muscle glucose uptake in overweight men after a short-term intervention.

However, the effect of GTE combine with brisk walking on FG levels was also not confirmed. We hypothesized that GTE combined with brisk walking might improve the FG levels, body weight, and waist circumference in overweight and obese men. Thus, the aim of this study were to examine the effects of GTE combined with brisk walking on the change in the FG levels, body weight, and waist circumference in inactive overweight and obese men under uncontrolled dietary conditions after 12-week intervention program and after 4 weeks of follow-up.

2. Methods

2-1. Study design, participants and intervention

The experimental design, statistical analyses, subjects and experimental intervention methods of this study are the same as those in Chapter 2, because these belong to the same experiment.

2-2. Testing

All participants visited the hospital 3 times: at baseline, at 12 weeks after the start, and at 16 weeks after the start (for the 4-week follow-up). Venous blood samples (5 mL) were obtained from all participants after fasting for 8-10 h (8:30-10:00 AM).

Body weight (BW), waist circumference (WC), systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measure at the center laboratory, Luohe Central of Hospital.

3. Results

3-1. General characteristics of the individuals

The demographic information of the subjects is shown in Table 6. There were no significant differences in the age, FG levels, BW, BMI, or SBP or DBP between the two groups. Two participants (one each in the GTE group and placebo group) dropped out of the study during the intervention period, due to gastrointestinal discomfort caused by the GTE or placebo. Another two participants (one each in the GTE group and placebo control group) dropped out of the study during the follow-up period, because of their jobs.

Table 6 Demographic data of participants

Variable	GTE group (n=12)	Placebo groups (n=12)	P
Age	42.5±9.82	37.2±7.17	0.163
FG(mmol/L)	5.26±0.83	5.16±0.87	0.853
Body weight (kg)	83.0±9.37	82.3±8.46	0.536
BMI	28.4±2.24	27.7±2.26	0.918
WC cm)	99.4±6.18	98.9±5.77	0.948
SBP (mmHg)	115±10.8	116±9.0	0.223
DBP (mmHg)	75±13.3	78±10.5	0.264

Note: BW: body weight; BMI: body mass index; FG: fasting glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure.

3-2. FG levels, body shape and other parameters

After 12 weeks, there were significant differences in the FG levels compared with before intervention in the both groups, no significant differences between groups (Table 7), but an increased trend after 4 weeks follow-up (Figure 14). After treatment, the GTE group only showed a significant reduction in the WC (Figure 15), with no significant difference from the placebo group in the body weight, BMI, or SBP and DBP (Table 8), and no change in the BW, BMI, and SBP, but an increased in DBP after 4 weeks follow-up. The placebo group showed no significant reduction in the WC, BW, BMI, or SBP and DBP. Table 8 showed that there was no significant group and group × time effects in the WC, BW, BMI, SBP and DBP in the both groups. A significant time effect was found for the FG levels.

Table 7 FG levels in ANCOVA after 12 weeks intervention

Variable	GTE group (n= 12)				Placebo group (n= 12)					
	Unadjusted		Adjusted		Unadjusted		Adjusted			
	Mean	SD	Mean	SE	Mean	SD	Mean	SE	F	*P*
FG (mmol/L)	5.64	0.751	5.60	0.139	5.66	0.985	5.70	0.139	0.256	0.618

Note: pre-intervention levels as covariates and post-intervention levels as dependent variables. Unadjusted: Values are expressed as mean ±standard deviation (SD). Adjusted: Values are expressed as mean ±standard error (SE). FG: fasting glucose

Table 8 FG levels and body shape parameters analysis of the participants during the experimental and follow-up periods

Variable	GTE group (n= 12)			Placebo group (n= 12)			P-value		
	Pre	Post	Follow-up	Pre	Post	Follow-up	Group	Time	Group ×Time
FG(mmol/L	5.26±0.246	5.64±0.253*	5.93±0.298#	5.16±0.246	5.66±0.253*	5.64±0.298#	0.730	0.000	0.358
BW(kg)	83.0±2.58	83.1±2.61	82.9±2.66	82.3±2.58	82.7±2.61	82.9±2.66	0.922	0.533	0.497
BMI	28.4±0.65	28.5±0.67	28.3±0.67	27.7±0.65	28.0±0.67	28.0±0.67	0.597	0.112	0.221
WC(cm)	99.4±1.79	98.2±1.87*	98.5±1.87	99.2±1.79	98.6±1.87	99.0±1.87	0.941	0.091	0.657
SBP(mmHg)	115±10.8	116±9.3	117±12.4	116±9.0	118±9.4	116±12.7	0.859	0.798	0.617
DBP(mmHg)	75±13.3	79±10.9	81±10.9*	78±10.5	81±11.4	77±12.8	0.863	0.119	0.139

Note: Values are expressed as mean ±SE. *, #, $p < 0.05$; * *P*-value for within-group comparisons in pre-and-post period; # *P*-value for within-group comparisons in post and follow-up. BW: body weight; BMI: body mass index; FG: fasting glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure.

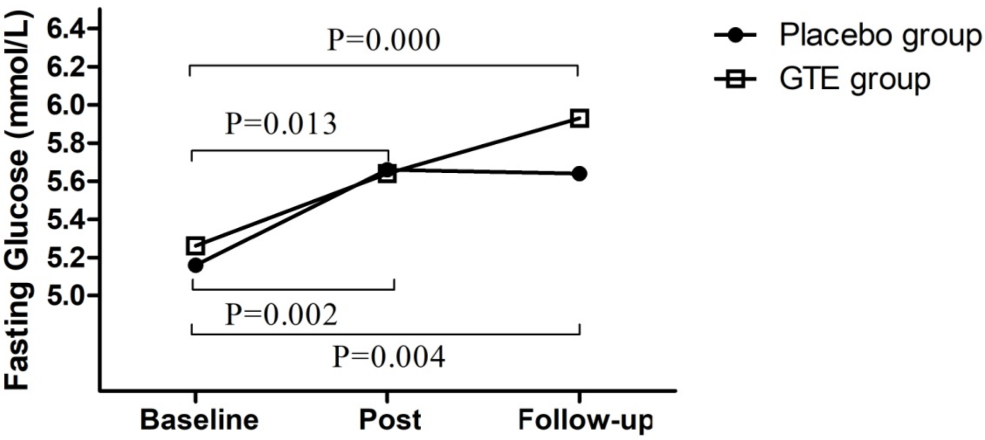
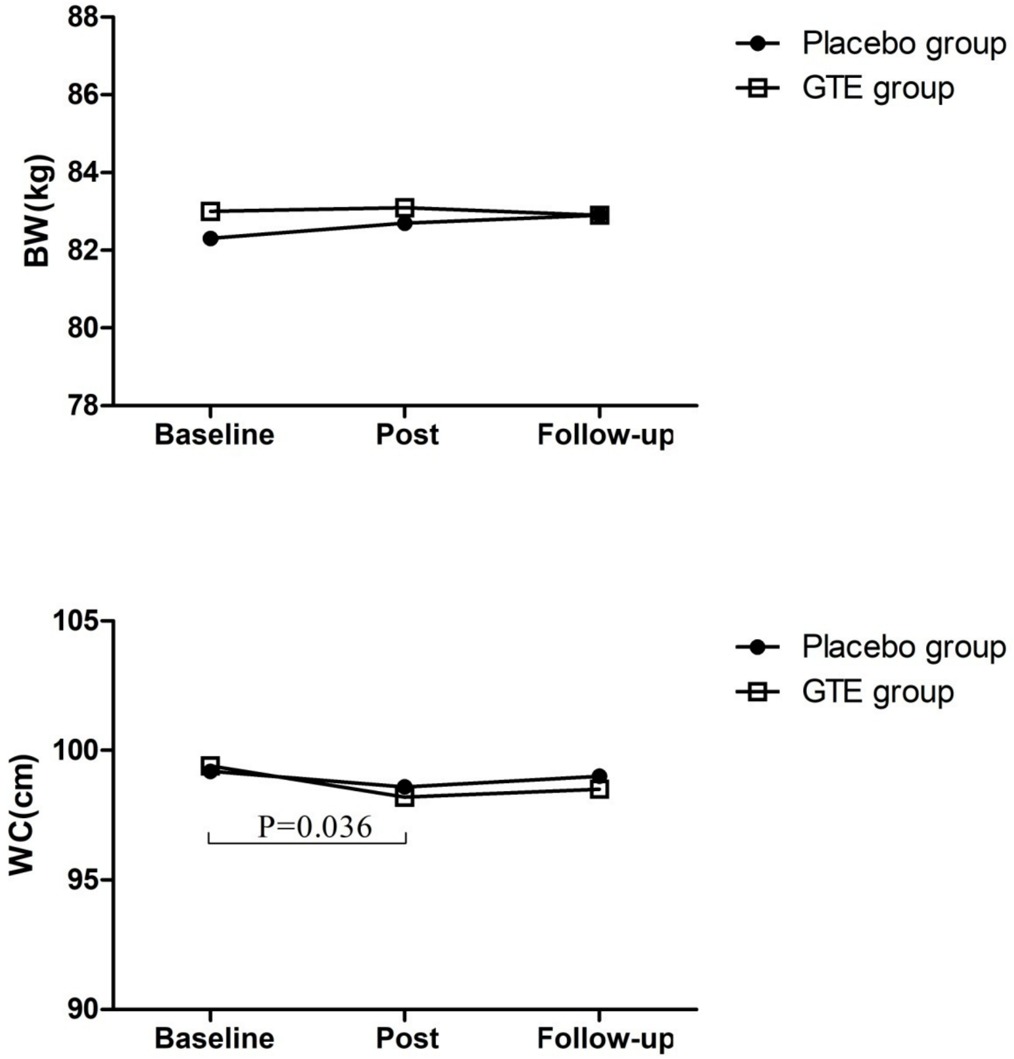


Figure 14 Effect of brisk walking combined with GTE on fasting glucose in overweight and obese men



Note: BW: body weight; WC: waist circumference

Figure 15 Effect of brisk walking combined with GTE on BW and WC in overweight and obese men

4. Discussion

In the present study, our comparison of the two groups showed that EGCG had no positive effect on the FG levels of overweight or obese men after a 12-week intervention program. We detected a significant reduction in the WC of the GTE group. However, we found no significant difference in the BW, BMI, SBP or DBP between the GTE and placebo groups after 12-week program, while the DBP was significantly increased in the GTE group. There were no changes in the BMI, WC, or SBP after 4 weeks of follow-up.

Of note, there was a significant increase in the FG levels in the present study. Studies (Kirwan, et al. 2017, Liu, et al. 2013) have reported that GTE was able to control the FG levels in humans. In addition, although it (Oja, et al. 2018) was reported that brisk walking was able to improve the FG levels in inactive healthy adults, we did not find a beneficial effect on the FG levels after the intervention program. The contrary result in the present study might have been due to the fact that all subjects were asked to maintain their dietary patterns during the intervention program. Previous studies reported that dietary patterns are strongly correlated with the fasting glucose levels in humans (Peluso, et al. 2017, Tian, et al. 2017). One the other hand, study by Tian et al. (Tian, et al. 2017) showed that most Chinese adults over-consume oil and salt. That might be the one reason.

Low-dose GTE might be another reason. Gaherman et al. (Gahreman, et al. 2016) reported no significant change in the FG levels of overweight men after 12 weeks of interval sprinting exercise combined with GTE (187.5mg polyphenols and 125 mg

EGCG) between or within groups. However, Brown et al. (Brown, et al. 2011) showed a beneficial effect (in comparison to baseline under daily living activities) on glucose-related marker levels in overweight and obese men after 6-week cross-over study in which subjects consumed a supplement with green tea catechins (800 mg/day). Thus, limitation and daily ingestion of EGCG should be considered. Further studies on the effects of GTE combined with brisk walking on the FG levels and body composition in overweight and obese men should be conducted.

We found a significant reduction in the WC of the GTE group. However, no significant reduction was observed in the BW or BMI in either group after the 12-weeks program. The results are contrary to those of a recent meta-analysis that showed that GTE has relatively little positive effect on BW loss (Hursel, et al. 2009). The mechanism underlying the reduction in BW by GTE might involve EGCG in the gastrointestinal tract decreasing the digestion and absorption of macronutrients or altering the gut microbiota and inhibiting the intestinal absorption of cholesterol and dietary fat (Yang, et al. 2016). These discrepant results between the present study and the conclusion of the meta-analysis may be due to the following reasons: first, only 300mg of EGCG was ingested each day in the present study. Rostamian et al. (Rostamian, et al. 2017) showed that a high daily dose green tea (1200mg/day) ingestion combined with aerobic exercise was indeed effective in helping to reduce the body weight in a 2-week intervention program. A previous study also reported that WC reduction in a GTE group was found following the consumption of EGCG (300 mg/day) (Hill, et al. 2007). Another possibility is that the dietary condition was uncontrolled in all participants. Bray et al. (Bray, et al. 2016) reported that dietary modification is an important strategies in the management of obesity, with a caloric intake of 1200-1500kcal/day in women or 1500-1800 kcal/day for men recommended for the management of obesity. Janssens et al. (Janssens, et al. 2015) showed that GTE had no effect on the BW in adults' men and women after a 12-week intervention program, in which the dietary condition of the participants was uncontrolled. Another important confounding factor may be the volume of exercise. There is evidence that increase the exercise volume is needed to lost weight (Bray, et al. 2016). This should be conducted in the future studies.

The present study was associated with several limitations. First, the sample size in this study was relatively small. Second, a relatively low dose of GTE was used. Third, we did not control the diet in the present study. Finally, an increased number of physiological parameters should be used in a future study.

In conclusion, the present study found that GTE combined with a brisk walking program had a negative effect on the FG levels, and no effects on BW, SBP, or DBP. This study indicated that there was no effect on FG levels in overweight and obese men consuming diets high in refined grains and fat. However, there was a significant change in the WC of the GTE group. These complex issues should be explored in more well-designed randomized controlled trials in the future.

Chapter 4. Effects of brisk walking combined with green tea extract on aerobic capacity and physical fitness function in overweight and obese men: A randomized, double-blinded, placebo-control trial

1. Introduction

Obesity is not only a major risk factor for chronic diseases, including metabolic syndrome, types 2 diabetes and some cancers, but also reduce the physical fitness functions in daily life (balance, endurance, walking steps) and the lifespan (Hita-Contreras, et al. 2013, Lai, et al. 2008, Pataky, et al. 2014). In addition, obesity is significant correlated with disability in daily life activities (Forhan 2009). Increased physical activity is an important component of lifestyle intervention for the management of obesity. Walking, especially brisk walking, has been described as a near perfect ‘‘exercise’’ and has been recommended by health organizations worldwide (Morris, et al. 1997, Nemoto, et al. 2007). A systematic review and meta-analysis by Hanson et al. reported that walking had a beneficial effect on body control, VO_{2max}, and aerobic capacity in individuals (Hanson, et al. 2015). Garnier et al. mentioned that 16 weeks of brisk walking was more effective than baseline for increasing cardiorespiratory fitness in moderately obese postmenopausal women (Garnier, et al. 2015). In addition, Willems et al. (Willems, et al. 2018) reported that green tea combined with brisk walking was able to reduce the respiratory exchange ratio and enhanced fat oxidation in women.

Green tea is one of the most popular beverages in the world, especially in Asia. Green tea is rich in catechins, among which epigallocatechin-3-gallate (EGCG) is the most pharmacologically active (Senanayake 2013). A previous study reported that green tea catechins combined with treadmill running was able to increase the endurance performance in mice (Minegishi, et al. 2018). Sae-tan et al. (Sae-Tan, et al.

2014) also showed that GTE combined with voluntary running exercise was more effective for increasing the expression of peroxisome proliferator-activated receptor in skeletal muscle in high-fat fed mice. In addition, Novozhilov et al. (Novozhilov, et al. 2015) showed that GTE combined with aerobic exercise was able to improve the aerobic exercise capacity and antioxidant system of erythrocytes. However, the effects of GTE combined with brisk walking on aerobic capacity and physical fitness in overweight and obese men.

Thus, we hypothesized that GTE combined with brisk walking might increase the aerobic capacity and physical fitness function in overweight and obese men. Therefore, the present study aimed to examine the effects of GTE combined with brisk walking on the change in (1) aerobic capacity and (2) the balance, strength and other physical fitness function after 12 weeks and 4-weeks follow-up in inactive overweight and obese men.

2. Methods

2-1. Study design, participants and intervention

The experimental design, statistical analyses, subjects and experimental intervention methods of this study are the same as those in Chapter 2, because these belong to the same experiment.

2-2. Testing

All participants visited the hospital 3 times: at baseline, at 12 weeks after the start, and at 16 weeks after the start (for the 4-week follow-up). Body weight was measured with the GAIA KIKO (Biospace, ACCUNIQ, Korea). Handgrip strength was measured to the nearest 0.1kg using an electronic hand scale (EH101, CAMRY, China). Sit-and-reach (SR), 8-foot up-and-go (8FUG), and eyes closed and one-leg-standing (ECOLS) were measured by relevant professional instruments in hospital. The 6-minute walking test (6MWT) was measured to indoor 30-m hospital corridor. The participants were instructed to walk the longest distance and as fast as possible in 6 minutes, and encouragement was given every minute during the test period. All parameters were measure at the center laboratory, Luohe Central of Hospital.

3. Results

3-1. General characteristics of the individuals

An analysis of the baseline characteristics of the participants showed no significant differences between the groups with regard to age, body weight, or BMI. Furthermore, there were no significant differences between the groups in the baseline 6MWT, 8FUG, HS, SR, and ECOLS results. (Table 9)

Table 9 Subject characteristics at baseline

Variable	GTE group (n= 12)	Placebo group (n= 12)
Age (years)	42.5±9.82	37.2±7.2
Body weight (kg)	83.0±9.37	82.3±8.46
Body mass index (BMI)	28.4±2.24	27.7±2.26
6MWT(m)	615±62.4	639±43.0
8FUG(s)	4.54±0.91	4.27±0.45
HS(kg)	45.7±3.78	45.9±6.58
SR(cm)	1.0±9.74	6.7±8.50
ECOLS(s)	10.6±5.55	16.3±25.24

Note: Values are expressed as mean ±SD. m: meters; s: seconds; kg: kilogram; cm: centimeter; 6MWT: 6 minutes walking test; 8FUG: 8-foot up-and-go; HS: Handgrip strength; SR: Sit-and-reach; ECOLS: eyes closed and one-leg-standing.

3-2. The between-group ANCOVA

The changes between groups were analyzed by an ANCOVA, with the pre-intervention levels as covariates and post-intervention levels as dependent variables. According to the results of the post-treatment ANCOVA, the 6WMT, 8FUG, and SR results of the two groups did not differ to a statistically significant extent (Table 10).

Table 10 Changes in the aerobic capacity and physical fitness after 12-week intervention

Variable	GTE group (n= 12)				Placebo group (n= 12)					
	Unadjusted		Adjusted		Unadjusted		Adjusted			
	Mean	SD	Mean	SE	Mean	SD	Mean	SE	F	*P*
6MWT (m)	655	70.1	666	9.3	674	49.4	663	9.3	0.097	0.759
8FUG (s)	4.27	0.732	4.18	0.09	3.86	0.323	3.95	0.09	3.402	0.079
SR (cm)	4.1	9.10	7.1	1.17	10.6	6.85	7.7	1.17	0.133	0.719

Note: pre-intervention levels as covariates and post-intervention levels as dependent variables. Unadjusted: Values are expressed as mean ±standard deviation (SD). Adjusted: Values are expressed as mean ±standard error (SE). 6MWT: 6 minutes walking test; 8FUG: 8-foot up-and-go; SR: Sit-and-reach; m: meters; s: seconds; cm: centimeter.

3-3. Repeat assessments

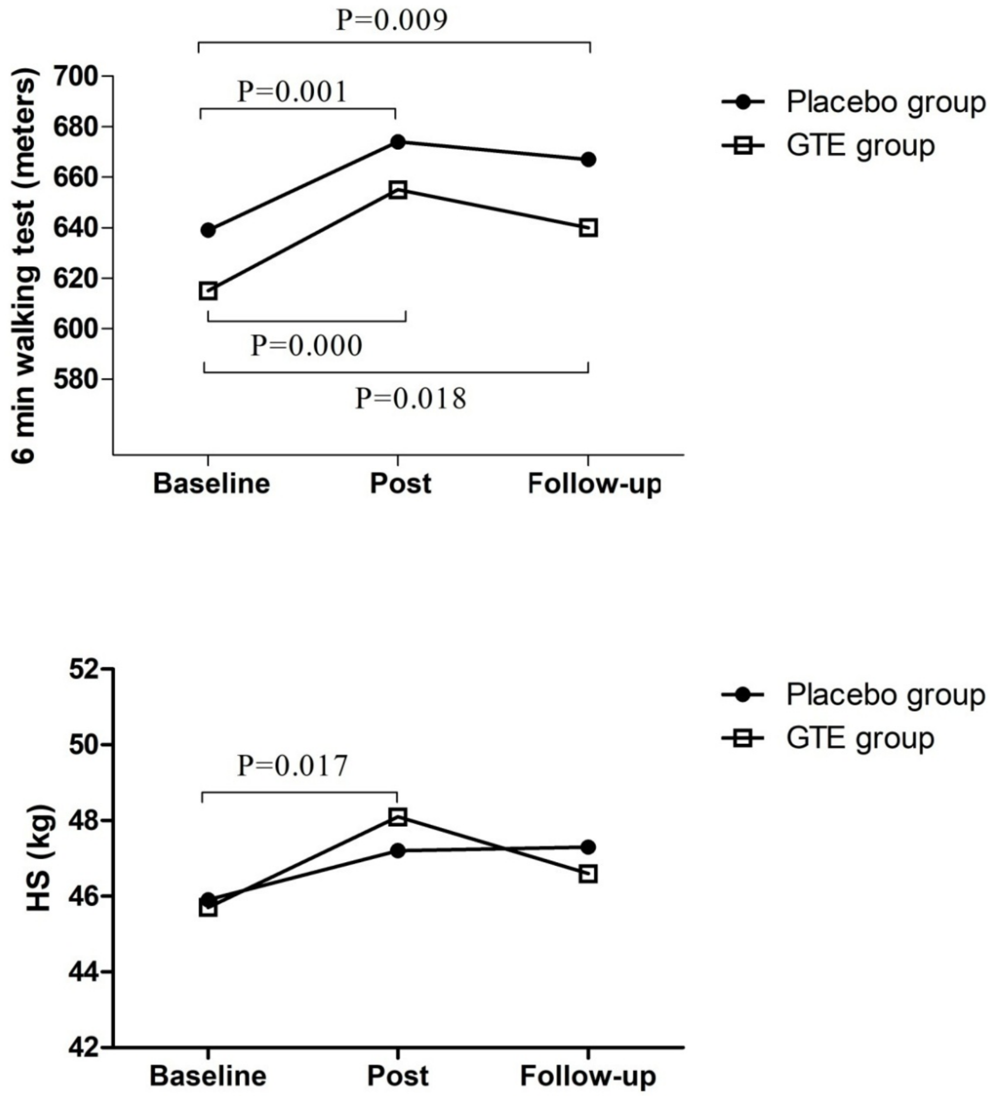
As shown in Table 11, no significant group, time, or group × Time main effects were found in ECOLS. Significant time main effects were found in the 6MWT, 8FUG, HS, and SR results. In the placebo group, there were significant changes in 6MWT and SR levels, and a down-ward trend after 4 weeks of follow-up. In the GTE group, the 6MWT and SR values were significantly reduced, and a down-ward trend was observed after 4 weeks of follow-up (Figure 16). There was a significant reduction in 8FUG levels after intervention; these values increased after follow-up. A similar result was observed in the placebo group. There were no significant groups or group×time main effects in any of the measurements in the GTE or placebo groups.

Table 11 Aerobic capacity and physical fitness analysis of the participants during the experimental and follow-up periods

Variable	GTE group (n= 12)			Placebo group (n= 12)			P-value		
	Pre	Post	Follow-up	Pre	Post	Follow-up	Group	Time	Group ×Time
6MWT(m)	615±15.5	655±17.5*	640.0±18.1&	639±15.5	674±17.5*	667±18.1&	0.318	0.000	0.832
8FUG(s)	4.54±0.207	4.27±0.163*	4.31±0.176#	4.27±0.207	3.86±0.163*	4.02±0.176#	0.193	0.000	0.565
HS(kg)	45.7±1.55	48.1±1.35*	46.6±1.59	45.9±1.55	47.2±1.346	47.3±1.59	0.988	0.023	0.479
SR(cm)	1.0±2.64	4.1±2.33*	3.4±2.42#	6.7±2.64	10.6±2.33*	9.5±2.42#	0.085	0.000	0.777
ECOLS(s)	10.6±5.55	17.0±6.86	19.7±6.11	16.3±5.55	20.4±6.86	20.9±6.11	0.672	0.082	0.650

Note: Values are expressed as mean ±SE. *, #, &p < 0.05; * *P*-value for within-group comparisons in pre-and-post period; # *P*-value for within-group comparisons in post and follow-up; & *P*-value for within-group comparisons in pre and follow-up. m: meters; s: seconds; kg: kilogram; cm: centimeter; 6MWT: 6 minutes walking test; 8FUG: 8-foot up-and-go; HS: Handgrip strength; SR: Sit-and-reach; ECOLS: eyes closed and one-leg-standing.

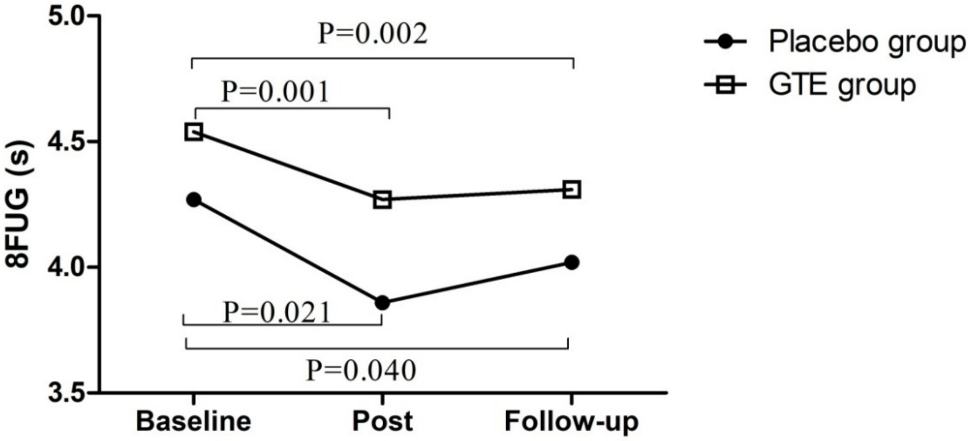
The results of the measurements of the aerobic capacity and physical fitness function are shown in Table 11. Regarding the physical fitness data, the GTE group exhibited significantly increased 6MWT levels, from 615±62.4 m to 655±70.1 m ($P < 0.01$), a significant change in 6MWT also observed in the placebo group, from 639±43.0 m to 674±49.4 m ($P < 0.01$). The ECOLS parameters' were not normally distributed (Shapiro-Wilk normality test: $P<0.01$). A Wilcoxon test showed no significant differences between the groups or within the groups.

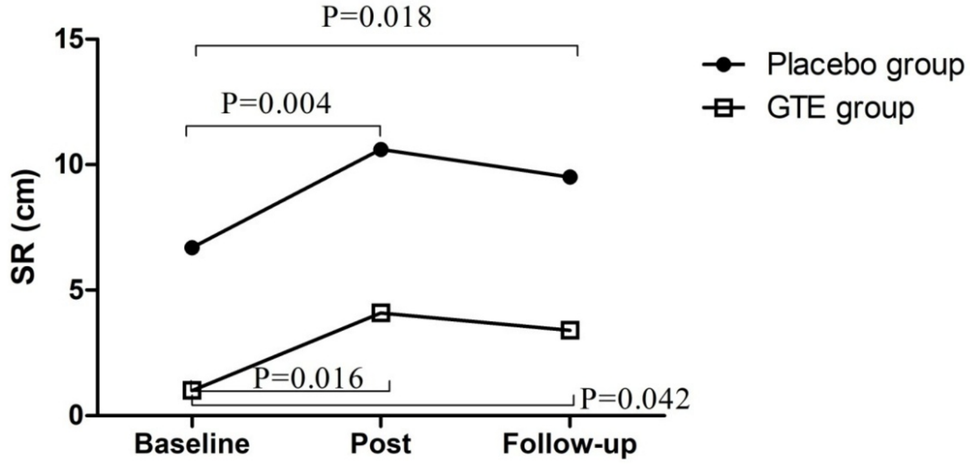


Note: HS: handgrip strength.

Figure 16 Effect of brisk walking combined with GTE on the 6min walking test and HS after 12 weeks intervention and 4-week follow-up

In the GTE group, the 8FUG value decreased from 4.54±0.21 s to 4.27±0.16 s (*P*< 0.01) after the 12-weeks intervention program, while HS and SR were increased from 45.7±1.55 kg to 48.1±1.35 kg (*P*< 0.01) and 1.0±2.64 cm to 4.1±2.33 cm (*P*<0.01), respectively. In the placebo group, the 8FUG value was reduced from 4.27±0.21 s to 3.86±0.16 s (*P*< 0.01), and there was a significant change in the SR level (*P*< 0.05) after the 12-week intervention program; these values tended to increase after the 4-week follow-up period (Figure 17).





Note: 8FUG: 8-foot up-and-go; SR: Sit-and-reach.

Figure 17 Effect of brisk walking combined with GTE on the 8FUG and SR after 12 weeks intervention and 4-week follow-up

4. Discussions

In the present study, we found significant changes in the 6MWT values of both groups after the 12-weeks intervention program and a downward trend after 4 weeks of follow-up. Animal and human studies reported that the mechanism underlying the improvement in endurance capacity by GTE combined with aerobic exercise was an increase in fat oxidation and a glycogen -sparing effect (Murase, et al. 2005, Sae-tan, et al. 2011). Minegishi et al. (Minegishi, et al. 2018) reported that a dietary intake of 0.5% green tea catechins increased fatty acid oxidation in skeletal muscle and improved the endurance capacity in mice. In a human study, Ichinose et al. (Ichinose, et al. 2011) reported a significant reduction in the respiratory exchange ratio during endurance training in healthy male adults after 10 weeks of consuming a supplement containing green tea catechins (572.8mg/day), while there was no change in a placebo group. This indicated that green tea catechins combined with aerobic exercise could increase whole body fat utilization during exercise. The findings of this study were contrary to those of a previous study, which showed that the daily intake of 570mg of tea catechins combined with twice week aerobic exercise significantly altered the aerobic capacity of healthy male adults (Ota, et al. 2016). Taken together, these studies suggest that the daily ingestion of high-dose GTE may improve aerobic capacity in overweight and obese men. Therefore, the discrepant results between the present study and the conclusion of the previous studies may be due to the following: first, the present study used a dose of only 300mg EGCG/day. The second important confounding factor may be the diet. We did not control the diet in the present study.

The present study found a significant increase in HS in the GTE group and a tendency toward an increase in the placebo group. Our study results were in line with the current double-blind controlled trials, which showed that a 10-week exercise program had a beneficial effect on muscle mass in overweight and obese women, even there was no significant difference between groups (Smith, et al. 2010). The significant change in the GTE group might have been because the ingestion GTE improved muscle recovery after exercise. A study by Panza et al. (Panza, et al. 2016) also showed that tea consumption and eccentric exercise was able to hasten the strength recovery for 24 h after exercise. Another study showed that tea catechins and walking had a significant effect on muscle strength and walking ability in elderly women (Kim, et al. 2013). The results of our study might have been due to a positive effect of GTE on muscle strength.

The results of the present study showed significant differences in the 8FUG and SR values of both groups after the 12-week intervention program and a downtrend in the follow-up period. The 8FUG and SR values did not differ between the GTE and placebo groups to a statistically significant extent. These results were in line with those of previous studies, which reported that aerobic exercise was able to improve the physical fitness function in adults (Melam, et al. 2016, Ribeiro-Alvares, et al. 2018). In addition, in the present study, we did not find a significant change in the ECOLS value after the 12-week intervention program. Although GTE has a positive effect on the body composition, muscle strength, and endurance capacity, no studies have focused on physical fitness in humans. We used these variables to assess the effects on the physical fitness function of the participants in our study. The effects of GTE combined with brisk walking might have been due to an indirect impact on body structure and posture, especially in overweight and obese adults.

The present study was associated with several limitations. First, the sample size was relatively small. Second, we did not set a group of control the dietary patterns of the subjects during the intervention period. Third, an increased number of physiological parameters should be used in a future study. A multi-arm trial with a larger study population should be conducted to confirm the results of the present study.

In conclusion, this study showed that the ingestion of GTE combined with brisk walking in inactive overweight and obese men for 12 weeks significantly increased their aerobic capacity and physical fitness, but no significant difference was observed between the groups. We found a significantly effect on the HS in the GTE group, which was more effective than brisk walking alone. In comparison to the post-intervention values, a downtrend was observed after the follow-up period. Further studies on the effects of exercise intensity, dietary modification and the daily-dose of GTE are needed to clarify the effects of GTE combined with brisk walking on the aerobic capacity and physical fitness function in overweight and obese humans.

Chapter 5. General Discussions and Conclusions

5-1. General discussions

In this study, firstly, the results presented in Chapters 1 showed that effects of brisk walking on body weight, waist circumference and lipid profile in overweight and obese adults was limited. A systematic review and meta-analysis showed that GTE combined with physical activity has no significant difference in the lipid profile in adults. The results from Chapter 2, the study showed that GTE combined with brisk walking significant reduced LDL-C levels and control the TC levels compared with the placebo group. The study also has demonstrated a more positive effect on the liver function than brisk walking alone. The results presented in Chapter 3 showed that GTE combined with brisk walking has a negative effect on fasting glucose in both groups, but the study showed a beneficial effect on waist circumference in the GTE group. The results from Chapter 4 showed that GTE combined with brisk walking was suggested to have positive effects on aerobic capacity, SR, and 8FUG in overweight and obese men and was more effective in improving HS than brisk walking alone; however, it had no effect on static balance.

As described in Chapter 1, there was a limited positive effect on body weight, body composition and lipid profile with brisk walking, and similar results in GTE combined with brisk walking study. There is growing evidence of the management of obesity benefits of brisk walking, including effects on lipid profile. However, we did not observe an effect of GTE combined with brisk walking on lipid profile and body shape. That may be due to few studies were included. Thus, in Chapter 2, we found GTE group resulted in a significant difference in the LDL-C and TC levels when compared to placebo group. A significant change in AST levels but only a downward trend in ALT levels was noted in the GTE group. These findings for ALT levels in the present study demonstrate that GTE combined with brisk walking has a beneficial effect on the liver function. However, there was only a down trend in the TG levels for the both groups, and an increased trend after follow-up period. The findings of this study are consistent with some of the previous studies in humans (Momose, et al. 2016) and suggest that effects may be more positive effect on the liver function than brisk walking alone. This study provides data to support the main mechanism of action for the improvement of lipid profile by GTE. The mechanism (Bartosikova, et al. 2018) underlying the reduction in plasma cholesterol levels by GTE might involve EGCG preventing the absorption of lipids and inhibiting digestive enzymes, with additional effects on the intestinal microbiota.

Compared with placebo group, we found that GTE combined with brisk walking was able to decrease the LDL-C and TC levels. Few studies focus on the effects of GTE combined with aerobic exercise on lipid profiles in overweight and obese adults under uncontrolled dietary condition (Gahreman, et al. 2016). The effect of GTE combined with brisk walking on LDL-C and TC levels change in this study agrees with the conclusions of a recent reviews (Deka, et al. 2011, Momose, et al. 2016), which showed that tea or tea extract can reduce the LDL-C and TC levels. However, the HDL-C levels has a significant increased for the GTE group and there was no change in placebo group after 12-week intervention. Although study (Yang, et al. 2012) reported that EGCG reduction the HDL -C levels, it was only showed a reduction trend in both groups. On the other hand, animal study (Liao, et al. 2016) demonstrated that the reason may be due to GTE increase the number of Bifidobacteria in gut and decreases the serum cholesterol level. A meta-analysis (Kodama, et al. 2007) reported that regular aerobic exercise can increase the HDL levels in human, and especially more effective in individuals with initially high cholesterol levels. In contrast, a study by Casella-Filho et al. (Casella-Filho, et al. 2011) showed that short-term moderate intensity exercise training has no effect on HDL-C levels in metabolic syndrome patients. Study (Wang, et al. 2017) has found that HDL-C levels are more sensitive to aerobic exercise than the other lipid profiles. However, there are several confounding factors in this study such as: aerobic exercise intensity, gender and physical condition (Cai, et al. 2016, Kelley, et al. 2006). Durstine et al (Durstine, et al. 2001) reported that significant increase in HDL-C levels was observed in the male exercisers (exercise energy expenditures of 1500 to 3000 kcal/week). The study also indicated that increased in exercise volume have more effect on this lipid fraction.

Our study showed that GTE combined with brisk walking was able to improve the liver function in inactivity overweight and obese men. Compared with placebo group, GTE has more beneficial effect on the ALT and AST levels. A meta-analysis (Huang, et al. 2016) reported that green tea consumption can reduce the risk of liver cancer. Another study (Masterjohn, et al. 2012) also showed that green tea catechins have a positive effect on nonalcoholic fatty liver disease. In addition, animal study (Park, et al. 2012) found that GTE has a potential positive effect on alcohol-induced liver damage. However, daily high-dose GTE also has a high risk of liver damage and even reduced death (Isomura, et al. 2016). 300mg EGCG/day was used in this study was based on the safety dose of GTE (EGCG), which recommended by a meta-analysis (Dekant, et al. 2017). Furthermore, accurate of daily dose GTE should be conducted to confirm the present studies results. Future investigations are needed to careful adjustment of confounding factors (such as: sample size, dietary patterns, exercise intensity, and with or without group training) affects the results.

Caloric reduction is an important component of weight loss. Many, but not all, studies (Ferreira, et al. 2016, Kapoor, et al. 2017) revealed that green tea or GTE ingestion was able to control or reduce the body weight. In our study (Chapter 3), we required all participants keep their dietary patterns, and most of the subjects were high-fat and excess cereal consumption in their dietary patterns (Song, et al. 2017). This is may be an important confounding factor for the study results, and this is also the considerable hypothetical premises. In addition, study (Astrup, et al. 2017) reported that dietary pattern have a strongly correlation with fasting glucose levels in human. Brown AL et al. (Brown, et al. 2011) showed that a beneficial effect on glucose-related marker in overweight and obese men after 6 weeks cross-over study of consuming a supplement with green tea catechins (800 mg/day) compared to the baseline under daily living activities. Despite study (Park, et al. 2014) showed that tea or tea extract has the potential beneficial effect on anti-diabetes. However, the result in our study was not supporting this conclusion. It may be due to the lower daily dose GTE, and there was an uncontrolled dietary pattern. This possibility should be investigated in the future animal and human studies.

In Chapter 4, we found a significant improve in 6MWT, 8FUG, and SR in both groups after 12 weeks intervention and there was a down trend after 4 weeks follow-up. There was a significantly increased in HS for the GTE group. Studies (Capodaglio, et al. 2010, Ettinger, et al. 1994) reported that excess weight imposes varieties of physical fitness function problems, such as: cardiorespiratory capacity, muscle strength, posture, walking, balance, and also increased the risk factors of activities of daily living and disability. A present study (Ekman, et al. 2013) also reported that the distance change in 6 minutes walking test could evaluate the cardiorespiratory capacity in obese subjects. Ota et al. (Ota, et al. 2016) reported that green tea beverage combined with graded cycle exercise was able to increase aerobic capacity in healthy male adults. In addition, study by Roberts et al. (Roberts, et al. 2015) showed that decaffeinated GTE combined with sub maximal exercise may potentiate improved exercise output. Therefore, the discrepant results between the present study and the conclusion of the previous studies may be due to the following: first, the present study used a dose of only 300mg EGCG/day. The second important confounding factor may be the diet.

In another study (Kim, et al. 2013) on elderly women trials, tea catechins and walking had showed a significant difference in muscle strength. Thus, we found a significant change in HS for the GTE group and a tendency toward an increase in the placebo group. Our study results were in line with the current double-blind controlled trials, which showed that a 10-week exercise program had a beneficial effect on muscle mass in overweight and obese women, even there was no significant difference between groups (Smith, et al. 2010). The results of our study might have been due to a positive effect of GTE on muscle strength.

5-2. Conclusions

In this thesis study, we demonstrated that green tea extract combined with brisk walking exhibited significant LDL-C and TC levels lowering properties in the overweight and obese men and also showed more effective improvement the liver function than brisk walking alone. In addition, we also confirm that GTE combined with brisk walking has a positive effect on aerobic capacity (6 minutes walking test), handgrip strength, sit and reach and reduce the risk of falling. However, there was no change in static balance in both groups. Although a negative effect on the FG levels was observed, the doctoral thesis has revealed some confounding factors. In comparison to the post-intervention values, a downtrend was observed after the follow-up period. The present doctoral thesis provides data to support the preventive effects of green tea combined with brisk walking on lipid profile, liver function, aerobic capacity and physical fitness in inactivity overweight and obese men.

Chapter 6. Limitations and Future directions

6-1. Limitations

Several limitations associated with the present study warrant mention. First, the sample size in this study was relatively small. Second, a relatively low dose GTE was used, and the effects of high-dose GTE were not evaluated. Thus, the replication of these findings in larger samples with high-dose GTE may be necessary in order to confirm the findings. Third, we did not control the dietary patterns and also did not investigate the diet in this study. Finally, more accurate testing should be used in the future study.

6-2. Future directions

It is clear that GTE ingestion and brisk walking has positive effects on LDL-C and TC levels in overweight and obese men, and brisk walking has a potential beneficial effect on HDL-C levels in overweight and obese men. However, GTE combined with brisk walking decreased the HDL-C levels for the GTE group. The mechanism is still unclear for GTE and its metabolites. Further studies are still necessary to establish that the role green tea catechins playing in cholesterol metabolism in gut and liver. The results presented in this study have showed a down trend in TG levels in both groups. Study reported that regular physical activity or exercise training can improve the TG levels, especially combination dietary control. Thus, future studies should to be identified.

The results of this thesis showed that GTE combined with a brisk walking program had a negative effect on the FG levels. However, there was a significant change in the

WC of the GTE group. These complex issues should be explored in more well-designed randomized controlled trials in the future. This study showed that the ingestion of GTE combined with brisk walking in inactive overweight and obese men for 12 weeks significantly increased their aerobic capacity and physical fitness, but no significant difference was observed between the groups. And results in this study also showed a positive effect on lower limb flexibility, handgrip strength, and reduce the risk of falling, but no effect on static balance. Therefore, high daily dose GTE and/or dietary modification will be considered for future studies.

In generally, further studies on the effects of exercise intensity, dietary modification and the daily-dose of GTE are needed to clarify the effects of GTE combined with brisk walking on the lipid profile, liver function, aerobic capacity and physical fitness function in overweight and obese adults. Furthermore, an increased number of physiological parameters should be used in a future study to confirm the effects on physical fitness function in overweight and obese men adults.

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