Effect of exercise training on lipid profiles in the elderly: A systematic review and meta-analysis of randomized controlled trials

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Abstract
Background and aims: There are many articles about the effects of different training methods on lipid profiles in the elderly. The objective of this study is to study the influence of training on the lipid profile in the elderly.

Materials and Methods: In this study, databases of PubMed, Embase, Scopus, ScienceDirect, Web of Science, SID, Magiran, and Google Scholar were searched. Intervention effects were presented as mean difference (MD) with a random-effects model. Subgroup analysis and sensitivity analysis were performed to study heterogeneity, following the primary screening of the full text of the articles.

Results: A total of 23 trials with 1654 individuals were included in the meta-analysis. Levels of high-density lipoprotein cholesterol (HDL-C) (MD = 0.47 mg/dL; P < 0.001, SE = 0.08, V = 0.01, 95% CI = 0.31 0.63, Z = 5.73, 16 trials), low-density lipoprotein cholesterol (LDL-C) (MD = -0.46; P < 0.001, SE = 0.11, V = 0.01, 95% CI = -0.68 -0.25, Z = -4.24), triglyceride (MD = -0.62; P < 0.001, SE = 0.12, V = 0.01, 95% CI = -0.86 -0.38, Z = -3.03, 20 trials), and total cholesterol (TC) (MD = -0.33; P < 0.001, SE = 0.09, V = 0.01, 95% CI = -0.52 -0.15, Z = -3.57, 16 trials) were investigated. Following sensitivity analysis and heterogeneity testing, the results were still strong and impressive.

Conclusion: Lipid profiles improved in training groups, indicating higher levels of HDL-C and lower levels of LDL-C, TC, and triglyceride. Overall, training leads to a better lipid profile. However, closer scrutiny seems necessary.

Keywords: Training, Triglyceride, Total cholesterol, HDL, LDL

Introduction
Interventions among older individuals have concentrated on cardiovascular disease (CVD) biomarkers (1). Training has been approved as a therapeutic measure with an important role in cardiac health and preventive medicine (2,3). Regular aerobic exercise appears to improve myocardial performance (3). Although normally ascribed to dyslipidemic profile and atherosclerosis (4), myocardial dysfunction has been reported in the absence of increased serum lipids (5). Because there is a relationship between myocardial disease and oxidative stress with dyslipidemic profile (5).

Lipids and lipoproteins as risk factors for CVDs in the elderly increase with age (1). Changes in circulating CVD markers are good indicators of the ideal impacts of training on cardiovascular health (6). A few examinations have indicated that the grown-ups with low degrees of high-density lipoprotein cholesterol (HDL-C) have a high risk of CVDs (7) and low-density lipoprotein cholesterol (LDL-C) was significantly correlated with CVDs and mortality (8). Observational studies comparing inactive and active groups confirm that training optimally decreases blood lipids (9). In some studies, ultra-endurance athletes had lower concentrations of LDL-C, higher concentrations of HDL-C, total cholesterol (TC), and triglycerides (TG) compared with a matched group (10).

Some reviews of the effect of training on the blood lipid have been published (11,12). One meta-analysis (13) reported decreases in LDL-C, TG, and TC with increases in HDL-C after training, other detailed reviews summarized different results. In this meta-analysis, different kinds of training with different intensity and duration were selected to evaluate the effect of training on lipid profile.

Therefore, considering 1) the lower than optimal prevalence of lipids and lipoproteins in the elderly 2) contradictory results of previous studies on the effect of lipids and lipoproteins in older people, and 3) lack of meta-analysis studies on the effect of training on lipids and lipoproteins in older people, this study was conducted to investigate the effect of training in on lipid profile in the elderly and provide recommendations for future research.

Materials and Methods

Review Article
Databases of PubMed, Embase, Scopus, ScienceDirect, Web of Science, SID, Magiran, and Google Scholar were searched. In literature searches of Cochrane Controlled Trials Registry, the following keywords were searched: “[exercise OR training OR physical activity OR Training] AND blood lipid OR blood fats OR lipedema OR Dyslipidemia OR hyperlipidemia OR hyperlipoproteinemia OR total cholesterol OR triglyceride OR high density lipoprotein cholesterol OR low-density lipoprotein cholesterol. Randomized controlled trials were included (RCTs) and compared with each type of the supervised training in terms of the outcome and reported means (or differences between means). Exclusion criteria were as follows: 1) RCTs that did not report enough data to complete meta-analysis; 2) Double-publications or subgroup analysis of trials.

Data extraction
Two examiners separately extracted all data. For the variables of interest, we extracted baseline, post-intervention mean and standard deviation, and sample sizes for intervention and control groups, following the Cochrane review protocols (14). Additional data obtained from abstracts included participants’ characteristics (gender, age, and duration of diabetes), year of publication, dietary intervention, follow-up time, and training characteristics (duration, type, severity, and frequency) (15).

Quality evaluation
Two authors individually assessed the methodological quality of the trials. The Cochrane risk of bias tool was used to assess the risk of bias (16): allocation concealment (selection bias), random sequence generation (selection bias), blinding of outcome assessment (detection bias), blinding of participants and personnel (performance bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other sources of bias. The experiments involved in the study had the following characteristics: random sequence generation (bias of selection), concealment allocation (bias of selection), blindness of participants and personnel (bias of performance), blindness of outcome assessment (bias of detection), incomplete outcome data (bias or apparent bias), selective reporting (bias of reporting) and other biases.

Statistical analysis
The analysis was completed using random-effect models (16, 17), and the consequences are shown as the weighted standard mean difference (SMD). The effect size of the intervention of each study was estimated in parameters between the control and training groups during the intervention. Heterogeneity was evaluated using I^2 index (14). Variables that may affect the association between training and outcomes included gender, kinds of training (resistance, aerobic, or a combination of both), mean age, sessions per week, period of study (continuous, weeks) (14). The funnel plot was used to assess the publication bias and the bias was statistically measured by the Egger methods (16). Trim-and-fill method was used to estimate the potential impact of unpublished studies on our results (16). All analyses were conducted by STATA version 12.0 (Stata, College Station, TX, USA).

Results
Twenty-three studies with 1654 participants were included in the analysis, 871 subjects in the training groups and 783 subjects in the control groups. Figure 1 indicates an overview of the search plan. Six studies were conducted on women and two studies on men and fifteen studies on both genders. The age of the participants ranged from 50 to 83 years. The number of sessions per week ranged from 3 to 5. The duration of interventions ranged from 7 to 52 weeks (Table 1).

Influence of training on LDL
The present meta-analysis shows that LDL levels significantly decreased by training (Figure 2) (MD = 0.47 mg/dL; P < 0.001, SE = 0.08, V = 0.01, 95% CI = 0.31 0.63, Z = 5.73, 19 trials), but the heterogeneity of the study remained significant (I^2 = 57%). In Figure 2, aerobic training significantly increased HDL levels (MD = 0.47 mg/dL; P < 0.001, SE = 0.15, V = 0.02, 95% CI = 0.18 0.76, Z = 3.2, I^2=53%), and resistance training significantly altered HDL levels (MD = 0.84; P < 0.001, SE = 0.24, V = 0.06, 95% CI = 0.37 1.31, Z = 3.52, I^2=36%)

Influence of training on HDL
The present meta-analysis shows that HDL levels significantly decreased by training (Figure 3) (MD = -0.3; P < 0.001, SE = 0.08, V = 0.01, 95% CI = -0.45 -0.14, Z = -3.81), but the heterogeneity of the study remained significant (I^2 = 68.8%). In subgroups, aerobic training significantly decreased LDL levels (MD = -0.49; P < 0.001, SE = 0.15, V = 0.02, 95% CI = -0.78 -0.21, Z = -3.36, I^2=72%), and resistance training significantly altered LDL levels (MD = -0.23; P < 0.19, SE = 0.18, V = 0.03, 95% CI = -0.59 0.12, Z = -1.31, I^2=0%).

Influence of Training on TC
The present meta-analysis shows that TC levels significantly decreased by training (Figure 4) (MD = -0.24; P < 0.001, SE = 0.07, V = 0.01, 95% CI = -0.38 -0.09, Z = -3.23), and heterogeneity of the study was 33%. In subgroups, aerobic training significantly decreased TG levels (MD = -0.35; P = 0, SE = 0.1, V = 0.01, 95% CI = -0.55 -0.15, Z = -3.38, I^2=52%), and resistance training significantly altered TG levels (MD = -0.33; P = -1.22, SE = 0.27, V = 0.07, 95% CI = -0.85 0.2, Z = -1.22, I^2=52%).
Figure 1. Flow chart of the study selection procedure.

Figure 2. Effects of training on HDL (mg/dL), forest plot showing pooled mean differences with 95% CI for 19 effect sizes obtained from 20 trials (two distinct effect sizes for various modalities were prepared by Ghamarchehreh et al) (30).

Figure 3. Effects of training on LDL (mg/dL), forest plot showings pooled mean differences with 95% CIs for 19 effect sizes obtained from 20 trials (two distinct effect sizes for various modalities were prepared by Ghamarchehreh et al) (30).
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Figure 4. Effects of Training on TC (mg/dL), forest plot showings pooled mean differences with 95% CIs for 15 effect sizes obtained from 16 trials (two distinct effect sizes for various modalities were prepared by Ghamarchehreh et al) (30).

Figure 5. Effects of training on TG (mg/dL), forest plot showings pooled mean differences with 95% CIs for 20 effect sizes obtained from 21 trials (two distinct effect sizes for various modalities were prepared by Ghamarchehreh et al) (30).
Table 1. Characteristics of the Included Studies

| Study                        | Age (y) (mean or rang) | BMI (kg/m²) (mean or rang) | Gender                  | Marker                                    | Activity/medical condition           | Duration (wk) | NT/NC | Exercise type, intensity and cointerventions                                      |
|------------------------------|------------------------|-----------------------------|-------------------------|-------------------------------------------|--------------------------------------|---------------|-------|-----------------------------------------------------------------------------------|
| Yoshizawa et al (18)         | (50-65)                | 23.7                        | Female only             | TC, TG, HDL-C, LDL-C                      | Sedentary/healthy                    | 8             | 12/13 | Resistance training/moderate/No                                                  |
| Vicente-Campos (2012)        | (62-67)                | NR                          | Male and female         | TC, TG, HDL-C, LDL-C                      | Sedentary/healthy                    | 28            | 22/21 | Aerobic training/vigorous/No                                                      |
| Takeshima et al (19)         | (60-83)                | NR                          | Male and female         | TC, TG, HDL-C, LDL-C                      | Sedentary/healthy                    | 12            | 18/17 | Progressive accommodating circuit exercise/vigorous/No                             |
| Takeshima et al (20)         | (60-75)                | NR                          | Male and female         | TC, TG, HDL-C, LDL-C                      | Sedentary/healthy                    | 7             | 15/15 | Endurance training (walking, dancing, 30 min), stretching, resistance training/vigorous/No |
| Nieman et al (21)            | (67.85)                | 23.7                        | Male and female         | TC, TG, HDL-C, LDL-C                      | Sedentary/healthy                    | 12            | 14/16 | Walking/moderate/No                                                              |
| Niedenscek et al (22)        | (C: 37.3±4.4, T: 66.4±2.3) | Female                      | TC, TG, HDL-C, LDL-C, CRP | Active/healthy                            | 12                                    | 22/20         | Skating/moderate/No                                                                 |
| Nicklas et al (23)           | (50-70)                | 25 to 40                    | Male and female         | TC, HDL-C, LDL-C                          | Sedentary/healthy                    | 20            | 36/29 | Calorie restriction and aerobic exercise/moderate                                  |
| Morgan et al (24)            | (60-70)                | NR                          | Female                  | TC, HDL-C                                | Sedentary/healthy                    | 15            | 14/15 | Walking/moderate/No                                                              |
| Morey et al (25)             | (60-89)                | 25 to 45                    | Male and female         | TC, HDL-C, LDL-C, TC, fasting glucose, insulin | NR/healthy                           | 52            | 180/122 | Enhanced fitness intervention/ NR/No                                                |
| Miyaki (2012) (26)           |                       | 60                          | Female                  |                                             | Sedentary/healthy                    | NR            | 11/11 | Walking and cycling/moderate/No                                                   |
| Kokkinos et al (27)          | (38.76)                | Male                        | TC, HDL, LDL-C, TC       | Sedentary/ Hypertension                   | 16                                    | 15/19         | Aerobic/exercise/moderate/No                                                     |
| Karstoft et al (28)          | (T: 60.8±2.2, C: 57.1±3.0) | NR                          | Male and female         | TC, HDL-C, LDL-C                          | NR/diabetes mellitus                 | 16            | 12/38 | Walking/moderate/No                                                              |
| Kadoglou et al (29)          | (64.1±9.2)             | Male                        | TC, HDL-C, LDL-C, TC     | Fasting glucose, insulin, HOMA-IR, HbA1c, Fibrinogen | NR/diabetes mellitus                 | 12            | 23/24 | Resistance exercise/vigorous/No                                                   |
| Ghamarcheheh et al (30)      | (T: 52.5±7.1, C: 54.4±6.6) | NR                          | Male and female         | LDL, HDL, TG                              | Sedentary                            | 8             | 13/13 | Three 45-min sitting per week at 55%-75% of heart rate reserve. RG participated in an 8 week |
| Ghamarcheheh et al (30)      | (T: 51.5±3.5, C: 54.4±6.7) | NR                          | Male and female         | LDL, HDL, TG                              | Sedentary                            | 8             | 13/13 | resistance training, three 45- min sitting per week at 50- 70% of HRM             |
| Finucane et al (31)          | (67.4±76.3)            | 27.2                        | Male and female         | HDL C, TG, LDL C, HbA1c Fasting glucose, TC | NR/healthy                           | 12            | 48/48 | Cycle ergometer/moderate/No                                                      |
| Fahlman et al (32)           | (74±5)                 | NR                          | Female only             | TC, HDL-C, LDL-C, TC, HDL-C               | Sedentary/healthy                    | 10            | 15/15 | 10 week of walking, 3 days/ week, 20 until 50 min/session, 70% of HRR            |
| Dalleck et al (33)           | (T: 55.4±3.2, C: 57.4±4.6) | Normal                      | Female only             | TC, HDL C, LDL C, TC, Fasting glucose     | Sedentary/healthy                    | 12            | 8/10  | NR/moderate/No                                                                   |
| Boardley et al (34)          | over 65                | NR                          | Male and female         | TC, TG, HDL-C, LDL-C                      | Sedentary/healthy                    | 16            | 33/15 | Resistance training and aerobic walking/moderate/No                                |
| Baldiucci et al (35)         | (C: 58.8±8.6, T: 58.8±8.5) | Male                      | TC, HDL-C, LDL-C, TC, TG, IR | Sedentary/ diabetes mellitus              | 52                                    | 288/275       | Aerobic and resistance training/moderate/No                                       |
| Baker et al (36)             | 58.2                   | NR                          | Male and female         | TC, HDL-C, LDL-C, VLDL-C                  | Sedentary/healthy                    | 20            | 20/14 | Aerobic training/vigorous/No                                                      |
| Bobeuc et al (37)            | (59.73)                | 26.2±6.2                    | Male and female         | HDL C, TC, TG, LDL-C                      | Sedentary/healthy                    | 24            | 17/12 | Resistance training/vigorous/ vitamins C/E supplementation                          |
| Sung et al (38)              | Over 70                | NR                          | Female                  | HDL C, LDL C, TC, Fasting glucose, HbA1c | NR/diabetes mellitus                 | 24            | 22/18 | Walking/moderate/No                                                              |

T: training group; C: control group; NR: not reported; HDL C: high-density lipoprotein cholesterol; LDL C: low-density lipoprotein cholesterol; BMI: body mass index; HbA1c: glycated hemoglobin A1c; TC: total cholesterol; TG: triglyceride; IL: interleukin, HOMA IR: homeostatic model assessment insulin resistance
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Influence of training on TG
The present meta-analysis shows that TG levels significantly decreased by training (Figure 5) (MD = -0.62; P < 0.001, SE = 0.12, V = 0.01, 95% CI = -0.86-0.38, Z = -5.03), and heterogeneity of the study was 33%. In subgroups, aerobic training significantly decreased TG levels (MD = -0.73; P = 0.001, SE = 0.16, V = 0.02, 95% CI = -1.04-0.43, Z = -4.73), and resistance training significantly altered TG levels (MD = -0.36; P = 0.07, SE = 0.2, V = 0.04, 95% CI = -0.76 0.03, Z = -1.83).

Subgroup Analysis
Subgroup analysis was performed for different training methods (Figure 6). In subgroups, study heterogeneity remained high. HDL levels increased and LDL, TC, and TG decreased in subgroup analysis.

Discussion
In this systematic review and a meta-analysis, the effect of training on the lipid profile in elderly people was investigated. According to meta-analyses, regular training resulted in changes in the levels of HDL-C (0.4 mg/dL), LDL-C (-0.18 mg/dL), TC (-0.33 mg/dL), and TG (-0.33 mg/dL). Furthermore, in the analysis of the subgroups, the resistance training produced changes in the levels of HDL-C (0.84 mg/dL), LDL-C (-0.23 mg/dL), TC (-0.32 mg/dL), and TG (-1.3 mg/dL). Several objective analyses have shown changes in lipid levels (39-41). Previous meta-analyses also suggested that training period or capacity could be correlated with improvement in lipid profile (40-42). For example, a meta-analysis indicated that each 10-minute increase in exercise duration corresponded to an increase of 1.4 mg/dL in HDL level. The mechanisms by which training has improved lipid profile levels are not yet clear. However, since adipocytokines are believed to cause dyslipidemia (43), developments in lipid metabolism are seemingly associated with changes in adipocytokine levels. A large-scale randomized controlled trial described that both HDL-C and adiponectin levels increased by intensive lifestyle intervention and that changes in HDL-C levels were associated with changes in adiponectin levels (44). A current meta-analysis also indicated that resistance training reduced leptin levels and improved adiponectin levels (45); therefore, resistance training can improve lipid profile through changes in adipocytokine levels. A meta-analysis suggested that training and drug interventions are potentially similar in preventing CVD (46). Since the lipid profile is a risk factor for CVDs (47) and regular training improves lipid and lipoprotein levels (48), improvement in lipid levels can prevent CVD. It is believed the mechanism by which workout prevents cardiovascular disorder improves vascular function. A meta-analysis confirmed that significantly elevated the pulse wave velocity (49). A cross-sectional study revealed that pulse wave velocity is correlated with HDL-C, CT, and TG values (50). Furthermore, a controlled clinical study that covered confirmed that the percentage change in LDL-C or CT all through surgical procedure was associated with the percentage change in heart rate throughout surgical operation (51). A randomized controlled trial, which has been covered in the current meta-analysis, examined the associated vascular function and confirmed that swimming training significantly improved carotid artery compliance (52). The current meta-analysis had several limitations. The limitations of this study were as follows: some studies have very small study groups which tend to have more serious effects. The design of educational interventions varies in duration and intensity. The analyzed population was heterogeneous in terms of clinical condition, age, publication bias. Further RCTs are required to investigate the effect of aerobic training on individuals with specific disease states using different practice times and frequencies (number of exercise sessions per week) to determine the frequency of practice and appropriate duration for specific disease cases.

Conclusion
Although the present meta-analysis and systematic review suggest that training represents a suitable strategy to improve lipid profiles in the elderly, a cautious
interpretation is warranted.

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Article editing: MG. Collecting information, writing preliminary proposals: MF, TB, and MF.

Conflict of Interests
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Ethical Considerations
In writing the article, the principles of publishing ethics have been observed.

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