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Coenzyme Q10 supplementation improves adipokine profile in dyslipidemic individuals: a randomized controlled trial

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Abstract

Background: In previous study, we found that coenzyme Q10 (CoQ10) improved glucolipid profile in dyslipidemic individuals, but the mechanism is not yet clear. Adipokines have been demonstrated to be vital targets of metabolic diseases. The hypothesis that adipokines mediate the association of CoQ10 on glucolipid metabolism needs to be further studied in human.

Methods: In this randomized, double-blinded, placebo-controlled trial, 101 dyslipidemic individuals were administered to 120 mg CoQ10 or placebo for 24 weeks. Anthropometric parameters, glucolipid profile, serum total adiponectin, leptin, and resistin were evaluated at baseline, week 12 and week 24.

Results: CoQ10 treatment significantly increased serum adiponectin levels at week 12 (165 [0, 362] ng/mL, $p < 0.001$) and at week 24 (523 [0, 1056] ng/mL, $p < 0.001$), which was significant different compared with placebo ($p < 0.001$). The increase of adiponectin was negative associated with decrease in index of homeostasis model assessment of insulin resistance (HOMA-IR, $r = -0.465$, $p = 0.001$), triglyceride (TG, $r = -0.297$, $p = 0.047$), and low-density lipoprotein cholesterol (LDL-c, $r = -0.440$, $p = 0.002$) at week 24 only in CoQ10-treated group. Resistin was reduced by CoQ10 only at week 24 (-1.19 [-4.35 , 0.00] ng/mL, $p < 0.001$), which was significant different compared with placebo ($p < 0.001$). Reduction of resistin was positively correlated with the change in HOMA-IR ($r = 0.343$, $p = 0.021$) and TG ($r = 0.323$, $p = 0.030$) at week 24 in CoQ10-treated group but not placebo group. Leptin was not influenced by CoQ10 treatment. Mediation analysis indicated that the improvement of HOMA-IR, TG and LDL-c by CoQ10 was mediated by adiponectin but not resistin.

Conclusions: Our study shows that CoQ10 ameliorates glucolipid profile and adipokines dysfunction in dyslipidemic patients in 24 weeks' intervention. The beneficial effect of CoQ10 on glucolipid profile was mediated by adiponectin. Trial registration: ClinicalTrials.gov, NCT02407548. Registered on April 3, 2015, <https://clinicaltrials.gov/ct2/show/NCT02407548>.

Keywords: Coenzyme Q10, Adipokine, Dyslipidemia, Clinical trial, Dietary supplement, Mediating effect

Introduction

Dyslipidemia is a risk factor of cardiovascular disease and vital component of metabolic syndrome. According to national data from 2013–2014, among Chinese adults aged 18 years or older, 28.5%, 26.3 and 25.8% had increased total cholesterol (TC), LDL-c and TG, respectively. And 20.4% had decreased high-density lipoprotein cholesterol (HDL-c) [1]. In developed country such as

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United States, Japan, and Korea, the incident rate of dyslipidemia is even higher [2–4]. Though the first-line medicine to treat dyslipidemia are statins, which efficiently decrease LDL-c and TC level and risk of atherosclerotic cardiovascular disease by inhibiting cholesterol synthesis. However, the increased risk of developing new-onset diabetes with statin-treatment raised concern of patients with dyslipidemia [5], especially those with borderline hyperlipidemia [6]. More safe and effective measures to improve dyslipidemia and concomitant metabolic disorders deserve investigation.

Accumulating evidences suggest that adipose tissue is an active endocrine organ. By secreting adipokines, such as adiponectin, leptin and resistin, it participates in the crosstalk of organs in various metabolic processes associated with dyslipidemia and hyperglycemia [7]. Adipokines can regulate the inflammation pathways that mediate the lipid metabolism [8]. Some adipokines such as adiponectin can modulate transcription factor such as peroxisome proliferator-activated receptors (PPARs) that regulate gene expression involved in lipid metabolism in multiple tissues [9]. Therefore, Adipokines have also become a pivotal target for treatment of obesity, dyslipidemia and hyperglycemia.

Coenzyme Q10 (CoQ10) is a lipophilic antioxidant, abundant in mammalian organs, such as heart, liver, and kidneys. It forms a crucial part of the electron transport chain in mitochondria which is essential for the production of ATP [10]. CoQ10 levels in the tissues and serum significantly decrease during aging [11] and many other pathological processes, such as myocardial disease [12], degenerative disease [13] and diabetes [14]. The effects of supplementation with CoQ10 in various diseases have been studied, but the results are inconsistent [15, 16]. In previous study, we found that CoQ10 can improve serum lipid profile and insulin resistance in dyslipidemic individuals, but the mechanism was not clear [17]. Is it possible that adipokines would mediate the effect of CoQ10 and improve glucolipid metabolism? Therefore, we measured and conducted further analysis of serum adipokines levels on the basis of our previous study, to clarify the effects of CoQ10 on adipokines and dyslipidemia in human.

Methods

Participants

This study used data from the previous randomized, double-blinded, placebo-controlled trial which examined the effects of CoQ10 supplementation on lipid and glycemic profile in dyslipidemic individuals, and a detailed protocol was published [17]. Briefly, 101 individuals were recruited from community health service centers in Guangdong province, China. Participants

were included if they were aged from 18 to 70 years and 2 or more of the following serum lipid parameters were abnormal: Serum fasting TC ≥ 5.20 mmol/L (200 mg/dL), fasting TG ≥ 1.70 mmol/L (150 mg/dL), fasting LDL-c ≥ 3.12 mmol/L (120 mg/dL), and fasting HDL-c ≤ 0.91 mmol/L (35 mg/dL). The exclusion criteria included serum fasting TC ≥ 8.0 mmol/L (309 mg/dL); fasting TG ≥ 4.5 mmol/L (395 mg/dL); history of cardiovascular diseases or atherosclerosis; hyperthyroidism or hypothyroidism; cancer; liver or renal dysfunction; consumption of any medicine or dietary supplement that influences lipid and glucose metabolism, inflammation, and oxidative stress.

Ethics

All protocols in the present study conformed to Helsinki's Declaration and approved by ethics committee of Sun Yat-Sen University. All subjects in this study were provided written informed consent prior to study entry. This trial had been registered at clinicaltrials.gov as NCT02407548.

Randomization and intervention

As previously described [17], eligible subjects were recruited and randomized to consume softgels of identical appearance with placebo or 120 mg CoQ10 (4 softgels per day, each contain 30 mg CoQ10, BYHealth Co Ltd, China) for 24 weeks. The softgels were identified by codes printed on the packaging bottles. Participants, investigators, and data analysts were blinded from the grouping information. Randomization was performed by an independent researcher using computer-generated random sequence that matching sex and age in blocks of 4. Participants were requested to maintain their usual diet and exercise habits and visit the study center every 4 weeks. Compliance was assessed by counting the empty pill containers returned by participants at each visit.

Data collection

Detailed method of data collection have been described in previous published article [17]. Briefly, at baseline, venous blood was collected in the morning after the subjects had fasted for 10–12 h. Then, a structured questionnaire was performed by trained research staffs via face-to-face interview. Information about socio-demographic data, medical history, uses of medications, dietary habits, and physical activities were collected. Blood samples and information collection were repeated at 12 weeks and 24 weeks after intervention.

Biochemical analyses

After fasting for 10–12 h, blood samples of the subjects were obtained in the morning at the beginning, 12th

week, and 24th week of the trial. The blood samples were centrifuged at $3000 \times g$ for 15 min before being separated serum and stored at -80°C until used. Biochemical parameters including concentrations of TC, TG, HDL-c, LDL-c, apolipoprotein A-1 (ApoA-1), apolipoprotein B (ApoB), blood glucose and insulin were measured with an automatic biochemical analyzer (Roche Group, Switzerland). HOMA-IR index was used to evaluate insulin resistance and calculated as $(\text{fasting insulin}[\text{mU/L}] \times \text{fasting blood glucose}[\text{mmol/L}]) / 22.5$ [18].

Fasting serum total adiponectin was measured using commercial ELISA kits (R&D Systems DRP300, USA). The kit can measure total (low, middle, and high molecular weight) human adiponectin in serum. The average intra and inter-assay coefficients of variation for adiponectin were 5.3% and 6.1%, respectively. Fasting serum leptin was measured by Human Leptin Quantikine ELISA Kit (R&D Systems DLP00, USA). The average intra and inter-assay coefficients of variation for leptin were 3.3% and 8.1%, respectively. Fasting serum resistin was measured with reagents of Human Resistin Quantikine ELISA Kit (R&D Systems DRSN00, USA). The average intra and inter-assay coefficients of variation for resistin were 5.5% and 6.2%, respectively. All ELISA experiments were conducted according to the manufacturer's instructions.

Statistical analysis

The sample size estimation was based on the primary outcome of TG, TC, LDL-c, and HDL-c as reported in the main paper [17]. Briefly, a sample size of 48 per arm was required to detect a 0.3 mmol/L (26.5 mg/dL) decrease in TG between groups at a type I error of 0.05 (two-tailed) and a type II error of 0.20 (power = 80%) [19]. The sample size estimation of TC, LDL-c, and HDL-c were less than 48. Therefore, at least 48 subjects were needed to include in each group. We conducted an intention-to-treat analysis, which included data from all participants who underwent randomization.

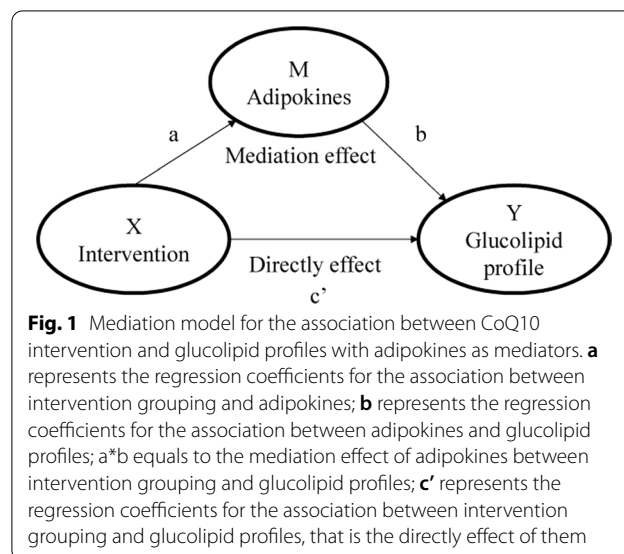
SPSS software (Version 19.0, IBM, Inc) was used for statistical analysis. Normality was tested by the Kolmogorov–Smirnov test for continuous variable. Abnormally distributed data were shown as median (with upper and lower quartiles). And differences of such variables between two group were assessed by Mann–Whitney U test. Data with normally distributed were described as mean values (with SD) or mean (with SE) as noted. Differences of such variables between groups were assessed using independent samples t tests. For the categorical variables, the chi-square test and percentage (%) were used. Pearson's correlation coefficients (r) were calculated to evaluate correlations between the changes in adipokines and glucolipid metabolic variables. A 2-tailed $p < 0.05$ was considered statistically significant.

To test whether the adipokines functioned as mediators between CoQ10 intervention and the improved glucolipid profile, we conducted mediation analysis according to Preacher and Hayes [20], which permits the assessing of multiple indirect effects simultaneously. Mediation analysis implements a series of regression analyses and estimates the total effects (c), direct effect (c') and the mediation effects ($a*b$) of a predictor (X) on an outcome of interest (Y) considering the role of one or more variables as mediators (M) (Fig. 1). The 95% confidence interval (CI) of effect were obtained via bootstrapping (5000 bootstrap samples). The 95% CI did not include zero indicating a significant effect. Mediation analyses were performed using Process v2.16.3 by Andrew F. Hayes [20]. All two-sided p values < 0.05 were considered statistically significant.

Results

General characteristics of the subjects

By using rapid lipid test with CardioChek PA Analyzer (PTS Diagnostics), we screened 127 qualified participants. After detailed examination, 101 were recruited and randomly assigned to either CoQ10 group ($n=51$) or placebo groups ($n=50$) at baseline. At week 12, two participants lost to follow-up in CoQ10 group for being absent from the schedule visits ($n=1$) and flatulence ($n=1$). Two participants in placebo group did not attend the schedule visits and withdrew. At week 24, one participants in CoQ10 group cannot meet the schedule visits and withdrew. Two participants withdrew for not coming the schedule visits ($n=1$) and flatulence ($n=1$) in placebo group. A total of 94 subjects (93.07% of those assigned) completed the study. But all participants who



underwent randomization were included in the analysis. The flow chart presented in Fig. 2 shows the allocation and the numbers of dropping out patients for each group.

The mean age of participants included in this study was 50.90 (SD, 9.95 years); 31.7% of them were male. At baseline, mean body weight was 64.26 kg (SD, 13.26 kg), BMI was 25.07 kg/m² (SD, 3.64 kg/m²). Intervention of 24 weeks did not change body mass significantly in both group [17]. At baseline, 56.4% of participants were prediabetics (defined as 7.0 > fasting blood glucose \geq 5.6 mmol/L or 126 > fasting blood

glucose \geq 100.8 mg/dL); 97.0% showed insulin resistance (defined as HOMA-IR index > 1); 64.3% had metabolic syndrome (defined according to National Cholesterol Education Program Adult Treatment Panel III [2005 American Heart Association] revised edition) [21], and the proportion of them were comparable between two groups. At the 24th week, less participants had prediabetes or insulin resistance or metabolic syndrome in CoQ10 group compared with baseline and placebo group ($p < 0.05$, Table 1).

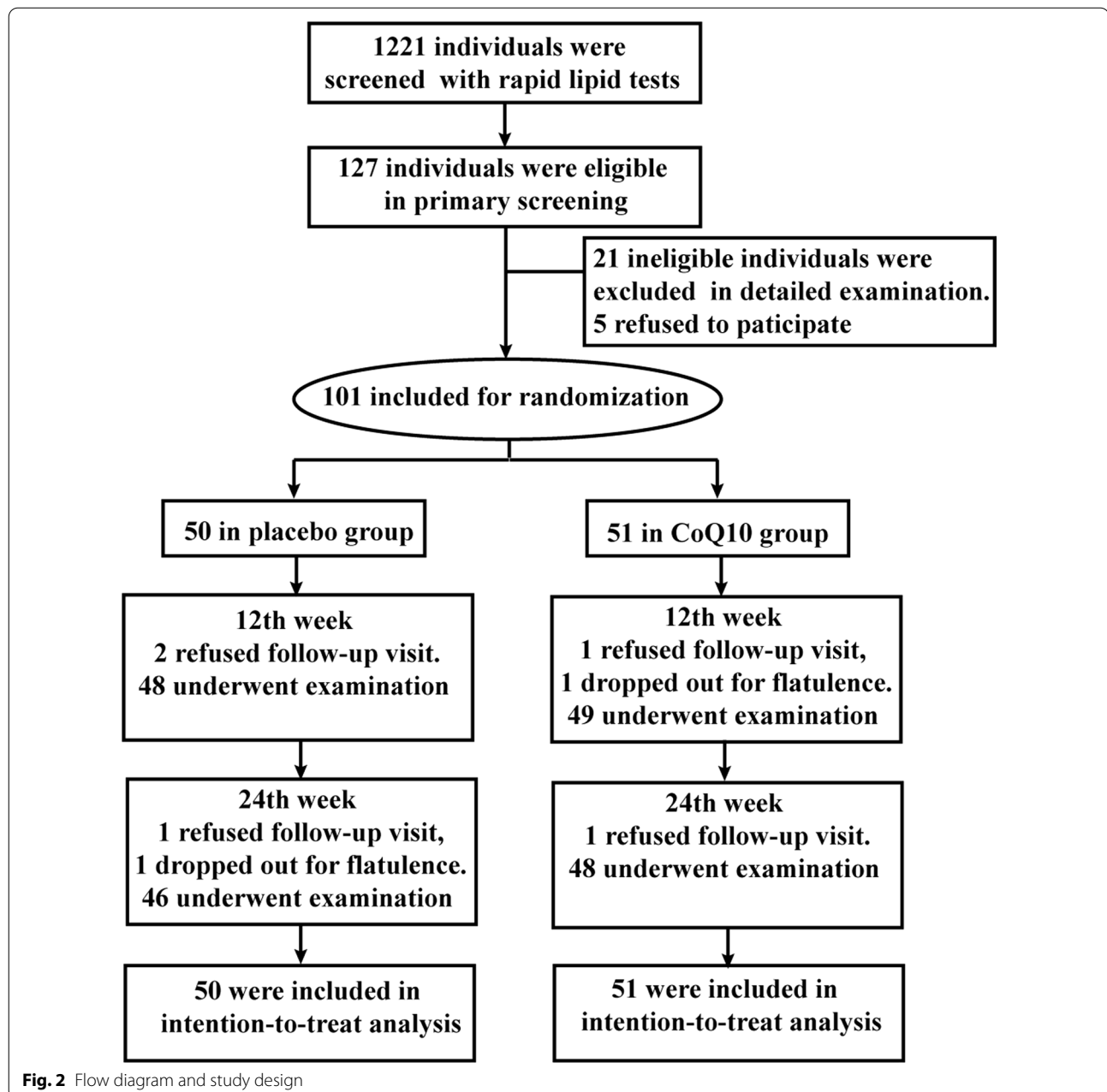


Table 1 Number of participants that with metabolic related disorders before and after intervention

Disorders n (%)	Placebo (n = 50)			CoQ10 (n = 51)			p_3^c	p_4^d
	Baseline	24-week	p_1^a	Baseline	24-week	p_2^b		
Prediabetes ^e	32 (64.0)	30 (60.0)	0.680	25 (49.0)	13 (25.5)	0.014	0.125	< 0.001
IR ^f	49 (98.0)	47 (94.0)	0.307	49 (96.1)	40 (78.4)	0.008	0.570	0.024
Mets ^g	30 (60.0)	28 (56.0)	0.685	35 (68.6)	18 (35.3)	0.001	0.365	0.037

^a p_1 values were calculated by chi-square tests for differences between baseline and 24th week in placebo groups

^b p_2 values were calculated by chi-square tests for differences between baseline and 24th week in CoQ10 groups

^c p_3 values were calculated by chi-square tests for differences between two group at baseline

^d p_4 values were calculated by chi-square tests for differences between two group at 24th week

^e Defined as 7.0 > fast blood glucose \geq 5.6 mmol/L or 126 > fast blood glucose \geq 100.8 mg/dL

^f IR, insulin resistance, define as HOMA-IR index > 1

^g Mets, metabolic syndromes, defined according to National Cholesterol Education Program Adult Treatment Panel III (2005 American Heart Association revised edition) definition

CoQ10 effects on the glucolipid profile

Changes of glucolipid parameters are displayed in Additional file 1: Table S1. Fasting blood glucose, insulin and HOMA-IR did not differ significantly between the intervention groups at baseline or week 12 [17]. At week 24, glucose levels were significantly decreased by the CoQ10 treatment (0.23 mmol/L [SE, 0.09 mmol/L]) compared to the placebo group. There were also significant differences in fasting insulin (2.86 mU/L [SE, 1.29 mU/L]) and the HOMA-IR (0.75, [SE, 0.34]) between the placebo and CoQ10 groups at week 24.

As for lipid profile, there were no significant differences in all markers between the two groups at week 0 and 12 [17]. At week 24, TG (0.33 mmol/L [SE, 0.15 mmol/L]) and LDL-c (0.30 mmol/L [SE, 0.13 mmol/L]) level significantly decreased in CoQ10 group compared to placebo group. ApoA-I/ApoB significantly increased (0.18 mmol/L [SE, 0.04 mmol/L]) in CoQ10 group compared to placebo group.

CoQ10 effects on serum adipokines

Furthermore, in order to investigate the adipokine changes by CoQ10 intervention, we detected three serum adipokines, which were adiponectin, leptin and resistin at baseline, week 12 and 24. As displayed in Table 2, concentration of three adipokines were not significant different between two intervention groups at baseline. In placebo group, adiponectin slightly but significantly decreased at week 12 (−78 [−308, 65] ng/mL, $p=0.018$), but did not significantly changed at week 24 (0 [−288, 145] ng/mL, $p>0.05$) compared to baseline. However, CoQ10 supplementation significantly increased serum adiponectin at week 12 (165 [0, 362] ng/mL, $p=0.001$)

Table 2 Effect of CoQ10 intervention on adipokines^a

Adipokines	Placebo group (n = 50)	CoQ10 group (n = 51)	p^b
Adiponectin, ng/mL			
Baseline	5578 (4471, 6939)	5503 (4415, 7561)	0.897
12 week	5648 (4210, 6847)	5668 (4626, 7740)	0.237
24 week	5899 (4308, 6842)	5890 (4848, 8224)	0.154
12-week change ^c	−78 (−308, 65)	165 (0, 362)	< 0.001
24-week change ^d	0.00 (−288, 145)	523 (0, 1056)	< 0.001
Leptin, ng/mL			
Baseline	10.35 (5.98, 16.82)	13.43 (6.09, 20.35)	0.446
12 week	8.37 (6.11, 14.71)	13.98 (6.16, 18.29)	0.156
24 week	8.28 (6.11, 15.21)	12.34 (5.75, 20.19)	0.153
12-week change	0.00 (−1.79, 0.84)	0.00 (−0.80, 0.86)	0.728
24-week change	0.00 (−3.16, 1.77)	0.30 (−0.10, 3.39)	0.177
Resistin, ng/mL			
Baseline	8.78 (3.79, 14.62)	11.40 (5.67, 14.45)	0.448
12 week	10.55 (4.48, 15.22)	12.14 (6.26, 14.60)	0.526
24 week	10.90 (4.56, 16.31)	6.20 (3.15, 13.15)	0.057
12-week change	0.12 (−0.45, 1.76)	0.09 (−0.13, 0.50)	0.868
24-week change	0.36 (−0.37, 1.64)	−1.19 (−4.35, 0.00)	< 0.001

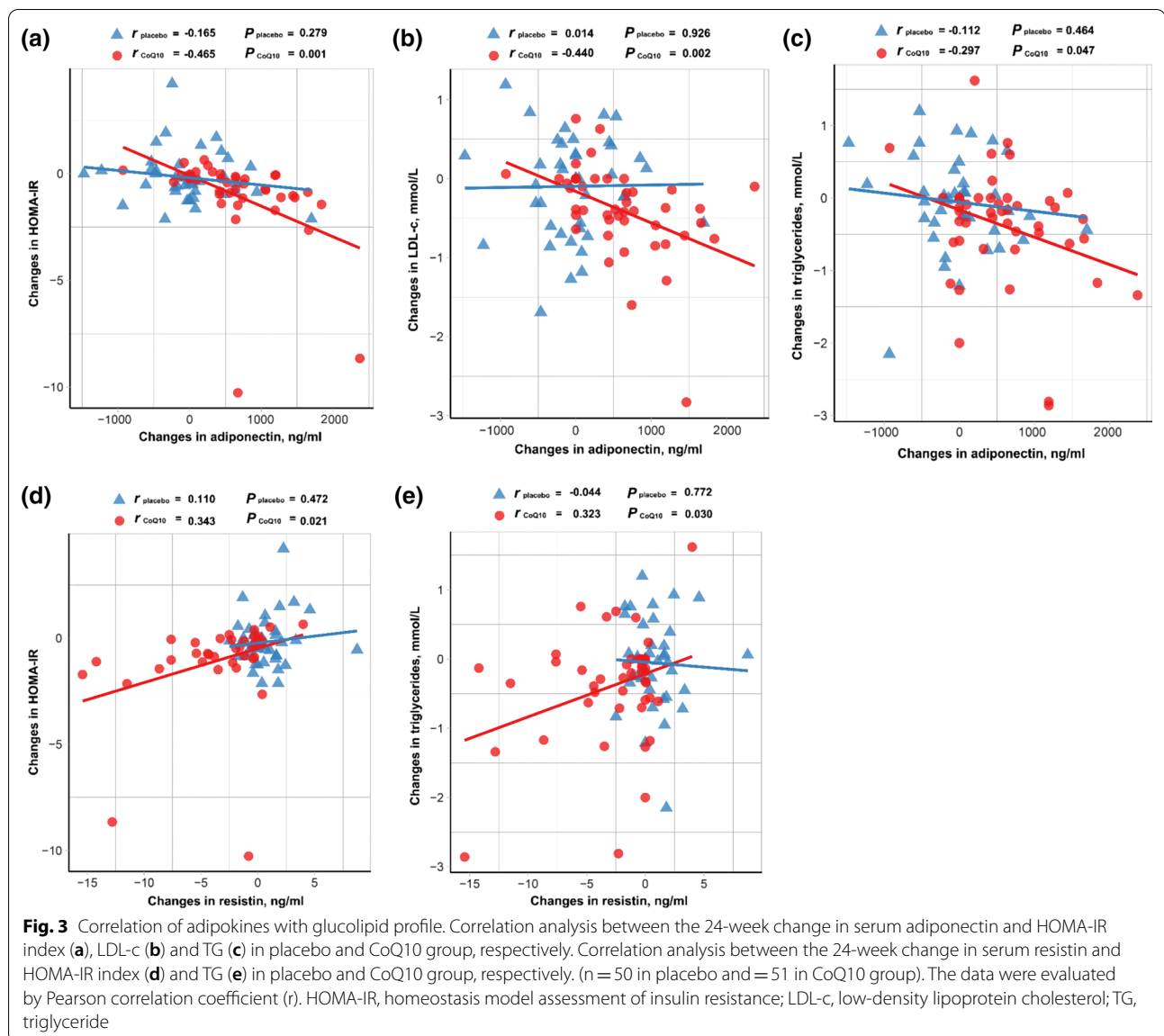
^a variables are presented as median (with upper and lower quartiles)

^b p value from comparison between two groups using Mann–Whitney U test at baseline, week 12, week 24, 12-week change and 24-week change, respectively

^c 12-week change = adipokine value at week 12—adipokine value at baseline

^d 24-week change = adipokine value at week 24—adipokine value at baseline

and week 24 (523 [0, 1056] ng/mL, $p<0.001$) compared to baseline. Change of adiponectin between two groups was significant different at week 12 ($p<0.001$) and week 24 ($p<0.001$). Change of resistin concentrations did not differ significantly between the intervention groups at week 12, but significantly decreased in the CoQ10 group



(−1.19 [−4.35, 0.00] ng/mL) compared to placebo group (0.36 [−0.37, 1.64] ng/mL) at week 24. Change of leptin levels did not differ significantly between two groups at week 12 or week 24.

Correlation of adipokines with markers of glucose and lipid metabolism

Moreover, we performed a correlation analysis to establish the relationship between adipokine profiles change and glucolipid related markers that had been improved in CoQ10 intervention study. 24-week change of adiponectin was negatively correlated with 24-week change of HOMA-IR ($r = -0.465$, $p = 0.001$), TG ($r = -0.297$, $p = 0.047$), and LDL-c ($r = -0.440$, $p = 0.002$) in CoQ10

group but not placebo group. There was no correlation between change of adiponectin and ApoA-I/ApoB at week 24 in both groups. Change in resistin concentration was positively correlated with the change in HOMA-IR ($r = 0.343$, $p = 0.021$) and TG ($r = 0.323$, $p = 0.030$) at week 24 only in CoQ10 group. There was no correlation between change of resistin and ApoA-I/ApoB or LDL-c at week 24 in both groups. Correlations of adipokines with markers of glucose and lipid metabolism are displayed in Fig. 3.

Mediating effects of adipokines

To further investigate the possible mechanism that adipokines mediated the relationship between CoQ10 and

glucolipid metabolism, we performed mediation analysis in significantly correlated adipokines and glucolipid related markers in CoQ10 intervention group. Firstly, we performed simple mediation analysis in the following path way: intervention → adiponectin → HOMA-IR, intervention → resistin → HOMA-IR, intervention → adiponectin → TG, intervention → resistin → TG, intervention → adiponectin → LDL-c. Grouping was set as independent variate X (placebo group = 0, CoQ10 group = 1). 24-week change of HOMA-IR or TG or LDL-c was set as dependent variate Y. Change of adiponectin or resistin between 24 weeks was set as mediator variate M.

As displayed in Table 3, CoQ10 was not directly associated with HOMA-IR or TG or LDL-c (all *p* of direct effect > 0.05). In contrast, the potential effect of CoQ10 on HOMA-IR was mediated by adiponectin (95% CI [−1.4, −0.21]) and resistin (95% CI [−1.19, −0.08]). However, effect of CoQ10 on TG was mediated by adiponectin (95% CI [−0.37, −0.01]) but not resistin (95% CI [−0.45, 0.04]). Analogously, adiponectin (95% CI [−0.32, −0.02]) but not resistin (95% CI [−0.22, 0.01]) mediated the effect of CoQ10 on LDL-c. As the effect of CoQ10 on HOMA-IR mediated by both adipokines, we further conducted a multiple mediation analysis which included both adiponectin and resistin as mediator variates. Results showed that total mediating effect of both adipokines (95% CI [−1.60, −0.29]) and the separate mediating effects of adiponectin (95% CI [−1.08, −0.16]) was significant. But the separate mediating effects of resistin (95% CI [−0.83, 0.05]) was not significant (Table 4).

Discussion

In our current study, supplementation with CoQ10 for 24 weeks not only improved serum levels of glucose, insulin, TG, LDL-c and ApoA-I/ApoB, but also increased

Table 4 The multiple mediation effects of adipokines on the association of CoQ10 with HOMA-IR^a

Markers	Directly effect	Mediation effect		
		Total	Adiponectin	Resistin
HOMA-IR	0.02 (−0.72, 0.76)	−0.76 (−1.60, −0.29)	−0.48 (−1.08, −0.16)	−0.29 (−0.83, 0.05)

^a The CI did not include zero indicates a significant effect. HOMA-IR, homeostasis model assessment of insulin resistance

serum adiponectin and decreased resistin. In CoQ10 group, change in adiponectin and resistin was correlated with the improvement of glucolipid profile. Moreover, mediating analysis indicated that CoQ10 improve glucolipid metabolism by affecting adiponectin.

As a lipophilic antioxidant, CoQ10 regulated lipid and glucose profile in a series of diseases, such as diabetes [22] and metabolic syndrome [23]. Consistently, our study also concluded that in Chinese dyslipidemia patients, long-term CoQ10 supplementation improved their insulin sensitivity and lipid profile. Though less powerful and cost-effective than clinical medication in lipid lowering and hypoglycemic therapy, CoQ10 has benefits on multiple risk factors of cardiovascular disease, including lowering blood pressure [17], blood glucose, lipids and HOMA-IR with few side effect. Therefore, CoQ10 is quite a good option for those who have moderate dyslipidemia with multiple metabolic disorders.

Leptin is a reliable marker of percentage of fat mass [24]. Increased circulating leptin was observed in insulin resistance and T2DM [25] and correlated positively with lipids levels [26]. In previous studies, CoQ10 supplementation significantly reduced leptin levels in individuals with non-alcoholic fatty liver disease [27] and type 2 diabetes [28], which were inconsistent with our study. The conflicting results may come from that the baseline serum

Table 3 The simple mediation effects of adipokines on the association of CoQ10 with glucolipid metabolic markers^a

Markers	Adiponectin		Resistin	
	Directly effect	Mediation effect	Directly effect	Mediation effect
HOMA-IR ^b	−0.15 (−0.86, 0.56)	−0.60 (−1.4, −0.21)	−0.25 (−0.98, 0.49)	−0.50 (−1.19, −0.08)
TG ^c	−0.16 (−0.50, 0.17)	−0.17 (−0.37, −0.01)	−0.16 (−0.49, 0.18)	−0.17 (−0.45, 0.04)
LDL-c ^d	−0.16 (−0.43, 0.11)	−0.14 (−0.32, −0.02)	−0.21 (−0.49, 0.08)	−0.09 (−0.22, 0.01)

^a The CI did not include zero indicates a significant effect

^b HOMA-IR, homeostasis model assessment of insulin resistance

^c TG, triglyceride

^d LDL-c, low-density lipoprotein cholesterol

level of leptin in the present study (median, 11.05 ng/mL) was much lower than previous two studies (median, 26.94 ng/mL in patients with non-alcoholic fatty liver disease and 23.51 ng/mL in patients with type 2 diabetes). Accordingly, participants in our study were much thinner (mean BMI was 25.07 kg/m²) than those two RCTs (mean BMI was 28.96 kg/m² in patients with non-alcoholic fatty liver disease and 28.99 kg/m² in patients with type 2 diabetes). Our results also shown that CoQ10 did not cause significant weight loss [17]. Therefore, it was not surprising to observe a less remarkable improvement in leptin in subjects who per se had moderate increased of leptin and BMI. However, we cannot totally rule out the possibility that CoQ10 can influence leptin secretion.

Several published RCTs had reported conflicting effect of CoQ10 in adiponectin in non-alcoholic fatty liver disease [27], hypertension [29] and type 2 diabetes [28]. The increase of adiponectin was parallel with the ameliorative effects on lipid peroxidation and glucose control [30]. Results from our present study were consistent with these trials. However, studies conducted in type 2 diabetes [31] and healthy, nonsmoking, sedentary men [32] found that CoQ10 supplementation for 8 weeks showed no improvement in adiponectin. The limited intervention time (less than 12 weeks) and mild illness condition may account for the negative results of adiponectin responded to CoQ10 supplementation.

In this study, we not only found that CoQ10 increased adiponectin, but also found that CoQ10 ameliorated glucolipid profile by mediating adiponectin. Adiponectin was thought as a protective adipokine. Extensive evidence have demonstrated anti-atherosclerotic, anti-diabetic, and anti-inflammatory activities that adiponectin possessed [33]. The gene expression of adiponectin is tightly controlled by a number of factors. PPAR- γ , which is expressed mainly in adipose tissue, is the major positive regulator of adiponectin gene expression. In contrast, inflammation factors such as tumor necrosis factor- α (TNF- α) inhibit adiponectin gene expression [34]. Interestingly, CoQ10 intervention can raise the expression of PPAR- γ in peripheral blood mononuclear cells of subjects with polycystic ovary syndrome [35]. CoQ10 can also partially attenuate the effect of TNF- α on PPAR- γ in HL-1 cardiomyocytes [36]. These results further suggested that adiponectin may be an important pathway and target of CoQ10 to improve lipid and glucose metabolic disorders. However, more studies were needed to further confirm them.

In human, resistin is synthesized predominantly by mononuclear cells inside and outside adipose tissues [37, 38]. It can increase the production of the proinflammatory cytokines such as TNF- α and interleukin-6 (IL-6) [39, 40]. As we known, chronic inflammation

was involved in the pathogenesis of obesity, type 2 diabetes and atherosclerosis. Therefore, resistin has been suggested as an important modulator and predictor of metabolic diseases [41, 42]. To our knowledge, this is the first study to investigate the effect of CoQ10 on resistin. Supplementation of CoQ10 for 24 weeks reduced serum resistin. Though change in resistin concentration was positive correlated with the change in HOMA-IR and TG in CoQ10 group, mediating analysis showed that resistin did not involve in the regulation mechanism of CoQ10 on these two parameters when considering adiponectin, which indicated that adiponectin is a more important mediator in regulating glucose and lipid. Another possible reason is that the reduction of resistin was accompanied by the improved of glucose and lipid. As resistin has been suggested as a marker of the severity of myocardium ischemic injury [43], the change of resistin by CoQ10 in dyslipidemic patients indicated a further decreased risk for them to develop atherosclerosis.

There were several limitations in this study. Firstly, we did not adjust the diet CoQ10 content as a cofactor in comparison of the effect between two groups. The CoQ10 content in Chinese food have not yet been well examined. However, according to Christine [44], the average CoQ10 intake in the Danish population was estimated to 3–5 mg/day, which was much less than our supplementation dosage (120 mg/d). Moreover, according to 3-day 24-h dietary record, the intake of energy, protein, total fat and total carbohydrate at baseline and during the 24-week intervention of two group was comparable [17]. Adjusted for 12- or 24-week physical activity and energy intake did not change the beneficial effect of CoQ10 on metabolic variables compared to placebo [17]. This suggested that CoQ10 intake by diet did not significantly affect the results of the intervention. Secondly, serum CoQ10 had not been estimated before and after intervention. But we assessed compliance by counting the empty pill containers and inquiry adverse reaction every 4 weeks. Thirdly, we did not deeply investigate the pathway behind CoQ10 and glucolipid metabolism in sophisticated experiment. But the mediation analysis revealed the important mediating role of adiponectin between CoQ10 and glucolipid metabolism. It provided the direction for further research.

Conclusions

In conclusion, we report that CoQ10 supplementation increase adiponectin and decrease resistin concentrations in dyslipidemic adults, which is correlated with the HOMA-IR and lipid profiles. Data suggested that the improvement of CoQ10 on glucolipid metabolism in dyslipidemic adults was partly by modulating adiponectin.

Abbreviations

ApoA-I: Apolipoprotein A-1; ApoB: Apolipoprotein B; CoQ10: Coenzyme Q10; HDL-c: High-density lipoprotein cholesterol; HOMA-IR: Homeostasis model assessment of insulin resistance; IL-6: Interleukin-6; LDL-c: Low-density lipoprotein cholesterol; PPARs: Peroxisome proliferator-activated receptors; TC: Total cholesterol; TG: Triglyceride; TNF- α : Tumor necrosis factor-alpha.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12986-022-00649-5>.

Additional file 1: Table S1. Effect of CoQ10 intervention on glucolipid profile.

Acknowledgements

Not applicable.

Authors' contributions

PZ, and KC conducted the research and wrote the manuscript; HG and XC designed the research; TH analyzed the data; XC had primary responsibility for the final content of the manuscript; all the authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All protocols in the present study conformed to Helsinki's Declaration and approved by ethics committee of Sun Yat-Sen University. All subjects in this study were provided written informed consent prior to study entry. This trial had been registered at clinicaltrials.gov as NCT02407548.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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