



Relationship between functional capacity and body mass index with plasma coenzyme Q₁₀ and oxidative damage in community-dwelling elderly-people



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ARTICLE INFO

Article history:

Received 12 October 2013

Received in revised form 26 January 2014

Accepted 28 January 2014

Available online 7 February 2014

Section Editor: Andrzej Bartke

Keywords:

Aging

Coenzyme Q₁₀

Cardiovascular disease

Fitness

Obesity

Physical activity

ABSTRACT

The impact of aging and physical capacity on coenzyme Q₁₀ (Q₁₀) levels in human blood is unknown. Plasma Q₁₀ is an important factor in cardiovascular diseases. To understand how physical activity in the elderly affects endogenous Q₁₀ levels in blood plasma, we studied a cohort of healthy community-dwelling people. Volunteers were subjected to different tests of the Functional Fitness Test Battery including handgrip strength, six-minute walk, 30 s chair to stand, and time up and go tests. Anthropometric characteristics, plasma Q₁₀ and lipid peroxidation (MDA) levels were determined. Population was divided according to gender and fitness. We found that people showing higher levels of functional capacity presented lower levels of cholesterol and lipid peroxidation accompanied by higher levels of Q₁₀ in plasma. The ratio Q₁₀/cholesterol and Q₁₀/LDL increased in these people. No relationship was found when correlated to muscle strength or agility. On the other hand, obesity was related to lower Q₁₀ and higher MDA levels in plasma affecting women more significantly. Our data demonstrate for the first time that physical activity at advanced age can increase the levels of Q₁₀ and lower the levels of lipid peroxidation in plasma, probably reducing the progression of cardiovascular diseases.

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1. Introduction

Aging is a multifactorial process resulting in damage of molecules, cells, and tissues, leading to a reduced efficacy of physiological functions with different pathological consequences (Corbi et al., 2012). Similarly, it has been reported that the aging process is associated with a higher oxidative stress (Ji, 2001), probably caused by reduced expression or deficiency in the activity of endogenous antioxidants (Miles et al., 2004a). Among other diseases, this leads to cardiovascular comorbidity and mortality (Deichmann et al., 2012).

Coenzyme Q₁₀ (Q₁₀) is a lipophilic compound synthesized by all aerobic organisms that is also obtained from the diet (Overvad et al., 1999). Q₁₀ is strongly involved in several important functions related to bioenergetics and protects against oxidative damage (Littarru and Tiano, 2007). Oxidative stress, through the generation of reactive oxygen species (ROS), is a normal process in the life of aerobic organisms (Banerjee et al., 2003). The lipid peroxidation degree determined by the levels of MDA in plasma has been then proposed as a biomarker

for oxidative stress (Mateos et al., 2005). Furthermore, Q₁₀ and MDA levels have been considered markers in the aging process (Kontush et al., 1999).

Physical activity has been associated with the generation of ROS (Banerjee et al., 2003). However, physical activity has also been shown as a preventive mechanism against oxidative stress. In fact, different training degrees could promote benefits by enhancing antioxidant capacity in humans (Corbi et al., 2012). Consequently, it has been proposed that the use of antioxidants may preclude the health-promoting effects of exercise in humans by reducing the induction of the endogenous antioxidant response (Ristow et al., 2009). We consider that this hormetic response to physical activity is responsible for some cardiovascular benefits such as decreased arterial stiffness, improved endothelial function and metabolic and clotting setting, and reduced body weight (Corbi et al., 2012). On the other hand, sedentarism and the related high body mass index have also been related to higher levels of oxidative stress (Beltowski et al., 2000; Roberts et al., 2006).

Despite the importance of Q₁₀ and lipid peroxidation as biomarkers for the aging process, no studies to our knowledge have been performed evaluating the oxidant/antioxidant response in plasma in relationship with functional capacity in elderly people. Therefore, the aim of the present study was to evaluate the relationship between levels of Q₁₀ and lipid peroxidation in plasma and

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functional capacity or body mass index among a sample of community-dwelling, elderly men and women.

2. Materials and methods

2.1. Participants and study design

The research was performed accordingly to the Declaration of Helsinki and was approved by the Bio-ethics Committee of Pablo de Olavide University. Volunteers were recruited between Feb. 1 and June 30, 2011, from different local associations or day centers in Seville, Spain. Participants signed an informed consent form prior to taking part in the study. The volunteers showing cognitive impairment or severe heart, liver or kidney diseases and those taking antioxidant or lipid-lowering medication were excluded from the study. Ninety one people accepted to participate in the study. Among them, 43 (19 men and 24 women) fulfilled the inclusion/exclusion criteria and were finally included in the study.

Volunteers participated in two separate sessions involving different procedures. The first session consisted of a validated questionnaire about socio-demographic variables including age or gender, as well as clinical characteristic variables (i.e. systolic and diastolic blood pressure and heart rate). At this point, blood samples for biochemical analysis were collected after overnight fasting. In the second occasion, the assessment of functional capacity and the estimation of BMI, body-fat mass and waist-hip ratio were performed.

2.2. Blood collection

Fasting blood for biochemistry was collected in a test tube containing heparin and immediately centrifuged at 4 °C and 3000 ×g using an eppendorf bench top centrifuge (Model 5810 R) for 10 min. Plasma fractions were stored at –80 °C until analysis.

2.3. Clinical chemistry analysis

Serum samples were analyzed by using a Reflotron plus (Roche Diagnostics, S.L.) that was calibrated and optimized according to manufacturer guidelines. Each serum sample was assayed for a lipid standard panel (triglycerides, total cholesterol and high-density lipoprotein (HDL)). Low-density lipoprotein (LDL) was determined using the Friedewald's formula (Friedewald et al., 1972).

2.4. Q_{10} determination

Q_{10} plasma levels were assessed using a previously described protocol (Fernandez-Ayala et al., 2005). After plasma extraction, 500 µl of a mixture of ethanol:isopropanol (95:5) was added to 500 µl of plasma. Samples were vigorously vortexed for 1 min. To recover Q_{10} , 5 ml of hexane was added, mixed by vortex and centrifuged at 1000 ×g for 5 min at 4 °C. The upper phase from three extractions was recovered and dried using a rotary evaporator (Büchi, Switzerland). Dried lipid extract was suspended in 1 ml of ethanol, dried again in a speed-vac and stored at –20 °C. Samples were suspended in the suitable volume of ethanol prior to HPLC injection. Lipid components were separated by a Beckman 166-126 HPLC system equipped with a 15-cm Kromasil C-18 column heated in a column oven set at 40 °C, with a flow rate of 1 ml/min and mobile phase containing 65:35 methanol/2-propanol and 1.42 mM lithium perchlorate. Q_{10} levels were analyzed with ultraviolet (System Gold 166) detector. Q_9 was used as internal standard. Q_{10} content was determined as nmol/l.

2.5. MDA determination

To assess plasma levels of MDA, we used the Cayman's TBARS Assay Kit following the instructions of the manufacturer.

2.6. Anthropometric and body composition measurements

Subjects' height and weight were measured and BMI estimated by dividing weight (kg) by height squared (m^2). Waist-to-hip girth ratio was also measured. Bio-electrical impedance (Tanita BF 350) was used to determine total body fat mass.

2.7. Functional capacity measurement

To assess functional capacity, we used different tests from the Functional Fitness Test battery (Rikli and Jones, 2013). We also performed the handgrip strength test, which is commonly used in elderly people (Aparicio et al., 2013; Carbonell-Baeza et al., 2011; Tomas-Carus et al., 2007) to evaluate upper-body muscular strength. This test was conducted with a digital dynamometer (TKK 5401 Grip-D, Takei Scientific Instruments, Tokyo, Japan). Participants maintained the standard bipedal position during the entire test with the arm in complete extension. Each participant performed the test twice with each hand, taking a 1-min resting period between measures. The best value of two trials was chosen as the test score for each arm (dominant and no dominant hand), and an average score of both hands was computed as bimanual Hand Grip Score. The grip position of the dynamometer was adjusted to each individual's hand size.

Motor agility/mobility was assessed by the Time Up and Go test (Rikli, 2001). Participant had to stand up from a chair, walk 2.44 m to and around a cone, and return to the chair in the shortest possible time. The best time of two trials (1-min resting period between each trial) was recorded.

To assess cardiovascular fitness, the 6MWT was used (Rikli, 2001). Subjects were instructed to walk at a fast and comfortable pace as far as they could in 6 min. The maximum distance (meters) walked was recorded as the test score. Participants were discouraged from talking during the test and were notified each passing minute. The 30s-STST (CST) test was used to assess lower-body strength (Rikli, 2001). Participants were instructed to perform the task starting and finishing in the seated position and were allowed a practice round before starting the test. The number of times within 30 s that the participant could raise to a full stand from a seated position with back straight and feet flat on the floor as fast as possible, without pushing off the arms was counted.

2.8. Statistical analysis

All tests were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics are presented as mean ± standard deviation (SD) for continuous variables and as frequencies and percentages for categorical variables. For the study purposes, data were organized in the two gender sub-groups (i.e. men and women), the fitness level (i.e. low level of fitness-people allocated under the percentile 50 of the test- and high level of fitness-people allocated in the percentile 50 or higher) and the body mass index (i.e. normal weight: those with a BMI between 18.5 and 24.9; overweight: those with a BMI between 25.0 and 29.9; and obese: those with a BMI of 30 and above). The distribution of the data was examined using the Kolmogorov–Smirnov test with Lilliefors correction. After confirming the normal distribution, differences between groups were determined using Student's *t*-test for independent samples. When more than two groups existed (i.e. for the body mass index), one-way ANOVA with Bonferroni post-hoc analyses was used to test the differences between groups. The significance level was set at $p < .05$ for all tests. Pearson correlations were performed to better depict the relationship between the different variables of the study. The level of relationship was determined based on the recommendations of Cohen (1988). A coefficient of between 0.1 and 0.29 was considered low, a coefficient between 0.3 and 0.49 was considered moderate, and more than 0.5 was considered high. Graphics were performed using Sigma Plot version 10.0.

3. Results

The age, body composition, biochemical profile and functional status of all the participants in the study separated by gender are shown in Table 1. Regarding the biochemical profile, men had lower levels of total cholesterol ($p = 0.022$), HDL-C ($p = 0.03$), LDL-C ($p = 0.001$) and greater Q_{10} /cholesterol ($p = 0.022$) and Q_{10} /LDL-C ($p = 0.021$) ratio in plasma than women. However, men also showed higher values in lipid peroxidation measured by MDA than women ($p = 0.034$). Concerning functional capacity, with the exception of the CST test, men showed better values in functional capacity (6MWT: $p = 0.050$, TUG test: $p = 0.050$ and Hand Grip Dominant arm test: $p = 0.01$) than women. No significant differences were found between men and women concerning body composition variables. In order to distinguish a division between lower and higher physical performance in the population, we determined the quartile values for the different functional capacity determinations within the total population and also separately for men and women (Table 2).

In Table 3, we show the differences between the levels of the biochemical variables in relationship with the different groups based on the fitness level. People showing low fitness level were allocated in the lower 50th percentile, and people with a high fitness level were allocated in the 50th percentile or higher except in the case of the TUG test, where higher percentile values (longer time spent in the test) indicate lower levels of physical capacity.

The highest levels of Q_{10} -related parameters were found in the participants showing the highest scores of cardiovascular fitness (total Q_{10} : $p = 0.005$, Q_{10} /Chol: $p = 0.017$, Q_{10} /LDL-C: $p = 0.006$). Although a trend toward greater levels of Q_{10} -related parameters was achieved in the group of participants with the high level of upper-body muscular strength, no statistically significant differences were found ($p = 0.061$). Furthermore, we did not find differences in the level of Q_{10} -related parameters between the participants showing lower and better values in lower body muscle strength (CST) or agility (TUG) tests (p between 0.8 and 0.9). On the other hand, those participants showing higher fitness

Table 2

Functional capacity of the participants in the study ($n = 43$).

Variables	Percentiles			
	25th	50th	75th	90th
<i>Total (n = 43)</i>				
6-min walking test (m)	402.00	446.12	528.50	587.50
Time up and go test (s)	6.45	7.57	9.19	10.81
Chair stand test (no. of stands)	13.00	15.00	17.00	19.00
Hand grip Dominant arm (kg)	17.00	25.20	36.75	51.02
<i>Women (n = 24)</i>				
6-min walking test (m)	400.50	426.00	487.50	564.50
Time up and go test (s)	8.29	7.07	12.25	17.50
Chair stand test (no. of stands)	12.25	14.50	16.00	18.00
Hand grip Dominant arm (kg)	17.15	21.50	26.37	30.10
<i>Men (n = 19)</i>				
6-min walking test (m)	420.00	485.00	570.00	600.00
Time up and go test (s)	5.68	7.08	8.95	9.94
Chair stand test (no. of stands)	14.00	16.00	18.00	21.00
Hand grip Dominant arm (kg)	35.00	40.30	50.00	54.00

T6MW: Six-minute walking test; TUG: Time up & go test; CST: Chair stand test Hand Grip Dominant arm: Hand Grip test execute by dominant arm.

levels in T6MW and CST tests reported lower MDA values ($p = 0.002$ and $p = 0.001$ respectively). Moreover, higher MDA levels were related to lower agility as determined by the TUG test ($p = 0.026$) (Fig. 1). In this test, people included in the higher percentile spent more time completing the test, showing then less agility. Additionally, a moderate positive relationship was found between the cardiovascular capacity of all the participants and Q_{10} -related parameters (total Q_{10} : $r = 0.399$, $p = 0.008$; Q_{10} /Chol: $r = 0.472$, $p = 0.001$; and Q_{10} /LDL-C: $r = 0.571$, $p = 0.001$ (not shown)). On the other hand, a negative relationship was found with MDA levels ($r = -0.490$, $p = 0.002$) (Fig. 2).

When the parameters were analyzed in relationship with the gender of the participants, we also found that cardiovascular capacity

Table 1

Characteristics of the participants in the study ($n = 43$).

Variables	TOTAL (n = 43)	Women (n = 24)	Men (n = 19)	p value
<i>Socio-demographic</i>				
Age (yrs.)	71.07 (6.22)	69.09 (5.30)	73.00 (6.21)	0.06
<i>Body composition</i>				
Weight (kg)	77.01 (19.47)	73.49 (20.71)	84.76 (17.24)	0.10
Height (cm)	169.27 (27.00)	156.33 (7.67)	166.89 (8.54)	0.00 ^a
Body mass index (kg/m ²)	29.94 (7.91)	30.05 (10.00)	30.07 (5.32)	0.99
Waist to hip ratio	0.87 (0.80)	0.85 (0.07)	0.90 (0.10)	0.13
% body fat	27.40 (11.91)	29.18 (14.41)	25.15 (7.48)	0.27
<i>Clinical variables</i>				
Systolic blood pressure	137 (25.76)	139.52 (16.86)	135.00 (31.31)	0.57
Diastolic blood pressure	76.72 (14.38)	77.84 (9.73)	75.83 (17.37)	0.65
Basal cardiac frequency	73.86 (11.49)	77.84 (9.73)	75.20 (12.09)	0.39
<i>Biochemical profile</i>				
Chol (mmol/l)	4.61 (1.43)	5.05 (1.12)	4.04 (1.58)	0.02 ^a
HDL-C (mmol/l)	1.37 (0.44)	1.48 (0.48)	1.19 (0.36)	0.03 ^a
LDL-C (mmol/l)	5.33 (1.47)	5.83 (1.30)	4.59 (1.49)	0.00 ^a
Q_{10} (nmol/l)	1155.92 (487.48)	1131.40 (498.99)	1186.90 (484.26)	0.71
Q_{10} /Chol-C (nmol/mmol)	301.18 (241.81)	227.05 (95.37)	394.81 (328.98)	0.02 ^a
Q_{10} /LDL-C (nmol/mmol)	242.38 (152.17)	196.19 (79.94)	300.71 (198.58)	0.02 ^a
MDA (μ M)	1.12 (0.76)	0.85 (0.63)	1.35 (0.79)	0.03 ^a
<i>Fitness level</i>				
6MWT (m)	461.45 (93.18)	438.23 (85.97)	490.77 (95.86)	0.05 ^a
TUG (s)	7.84 (1.74)	8.29 (1.61)	7.27 (1.77)	0.05 ^a
CST (no. of stands)	15.09 (2.88)	14.54 (2.80)	15.78 (2.85)	0.16
Hand grip dominant arm (kg)	29.59 (12.89)	21.81 (5.80)	39.42 (12.73)	0.01 ^a

Q_{10} : Coenzyme Q_{10} total levels; Chol: Total Cholesterol; LDL-C: low density lipoprotein; HDL-C: High density lipoprotein; MDA: malondialdehyde T6MW: six-minute walking test; TUG: Time up & go test; CST: Chair stand test; Hand Grip Dominant arm: Hand Grip test execute by dominant arm; p value: p value from *t*-test for independent measurements (a).

Table 3
Differences in biochemical variables based on fitness level (n = 43).

Variable	T6MW (m)		TUG (s)		CST (no. of stands)		Hand grip Dominant arm (kg)	
	p < 50 (n = 21)	p ≥ 50 (n = 22)	p < 50 (n = 23)	p ≥ 50 (n = 20)	p < 50 (n = 20)	p ≥ 50 (n = 23)	p < 50 (n = 9)	p ≥ 50 (n = 10)
Q ₁₀ (nmol/l)	948.9 (410.7)	1409 (413.6) ^a	1163 (517.5)	1184 (447.1)	1122 (507.1)	1185 (479.2)	1184 (465.8)	885.5 (660.4)
Chol (mmol/l)	5.124 (1.131) ^a	4.179 (1.541)	4.772 (1.091)	4.358 (1.344)	4.615 (1.524)	4.610 (1.382)	4.899 (1.323) ^a	3.881 (1.508)
LDL-C (mmol/l)	5.515 (0.9787)	4.909 (1.573)	5.213 (1.029)	5.156 (0.9691)	5.190 (1.704)	5.375 (1.349)	5.590 (1.476) ^a	4.295 (1.201)
Q ₁₀ /Chol (nmol/mmol)	212.2 (118.5)	402.0 (294.3) ^a	272.9 (178.8)	292.8 (245.3)	297.5 (255.6)	304.4 (235.0)	279.2 (203.5)	373.7 (343.6)
Q ₁₀ /LDL-C (nmol/mmol)	179.0 (80.33)	315.2 (174.4) ^a	242.1 (130.6)	261.0 (174.2)	249.2 (178.3)	245.3 (125.0)	233.1 (143.3)	273.0 (183.5)

Values are presented as Mean (SD); Q₁₀: Coenzyme Q₁₀ total levels; Chol: Total Cholesterol; LDL-C: low density lipoprotein; T6MW: Six-minute walking test; TUG: Time up & go test; CST: Chair stand test Hand Grip Dominant arm: Hand Grip test execute by dominant arm; a: p value < 0.05 in regard of the different fitness test.

determined by the T6MW test positively correlated with the level of Q₁₀-related parameters and negatively with lipid peroxidation levels in both men and women (Table 4). We found a high positive relationship between cardiovascular fitness and all of the Q₁₀-related parameters, particularly in women (total Q₁₀: r = 0.585, p = 0.003; Q₁₀/Chol: r = 0.540, p = 0.006; Q₁₀/LDL-C: r = 0.582, p = 0.003). However, no significant relationship was found in men (Fig. 2). On the other hand, a strong negative relationship was found for men and women when MDA and cardiovascular capacity were correlated (Fig. 2). Furthermore, MDA values also showed a correlation with the score in the TUG test in men (p = 0.024) and the CST test in both men (p = 0.048) and women (p = 0.050) (Table 4).

When the lipid profile was analyzed in the total sample of the population, those volunteers with reduced upper body strength showed higher levels of cholesterol (p = 0.047) and LDL-C (p = 0.016) compared to those with high levels of upper-body strength (Table 3). When the analysis was performed separately by gender (Table 4), men showing better scores in the cardiovascular test also showed reduced levels of cholesterol (p = 0.042) and LDL-C (p = 0.049) when compared with their peers with low levels of cardiovascular fitness. We also noted a trend toward decreasing cholesterol and LDL-C levels in women in this test, but the difference was not statistically significant.

The effects of the body mass index on Q₁₀-related parameters, MDA values and lipid profile within the total sample of the study were also determined (Fig. 3). Obese participants had lower Q₁₀ levels than those participants in the normal weight group (p = 0.010) or overweight group (p = 0.043). Moreover, the Q₁₀/Cholesterol and Q₁₀/LDL-C ratios were also lower in the obese group compared with control and overweight groups (Fig. 3). These participants also showed higher MDA values when compared with those in the overweight group (p = 0.020). On the other hand, BMI did not influence the lipid profile-related variables (Fig. 3). We also found a strong negative correlation between total Q₁₀ (r = -0.553, p = 0.002), Q₁₀/chol (r = -0.434, p = 0.021) and Q₁₀/LDL-C (r = -0.552, p = 0.001) and BMI in the total population (Fig. 4). On the other hand, a positive correlation was found between MDA (r = 0.444, p = 0.016) and BMI (Fig. 4). Women categorized in the normal weight group showed higher levels of Q₁₀-related parameters when compared to those in the obesity group (total Q₁₀: p = 0.016, Q₁₀/Chol: p = 0.007, Q₁₀/LDL-C: p = 0.004). Additionally, obese women showed higher MDA values than overweight and control groups (p = 0.035). Surprisingly, this significant influence was not found in men, although a similar trend was found in total Q₁₀, Q₁₀/Chol and MDA levels (Table 5, Fig. 5).

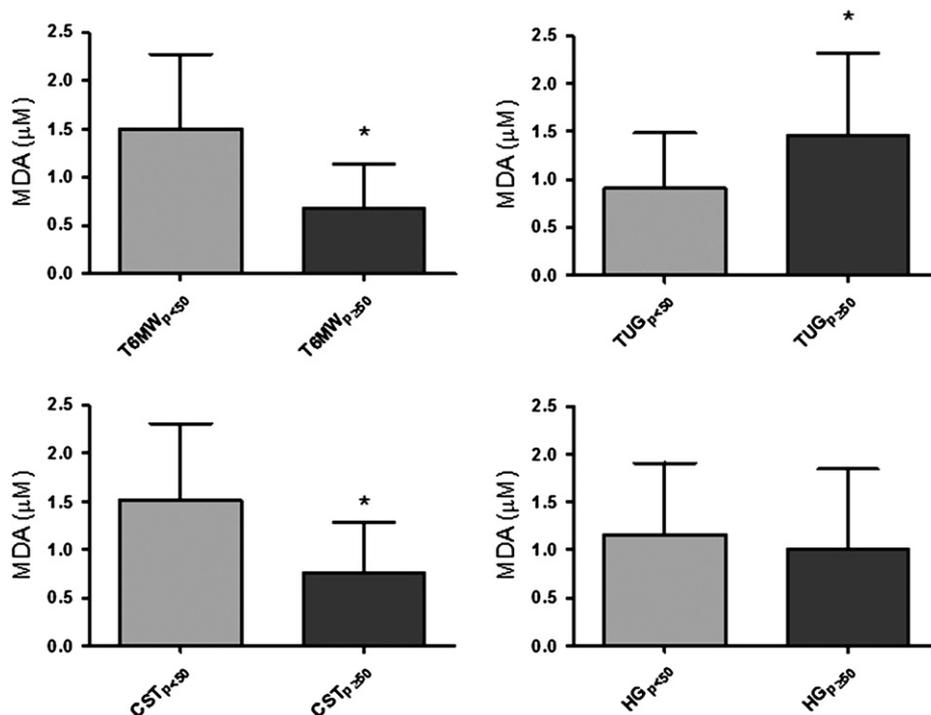


Fig. 1. Relationship of functional capacity and lipid peroxidation. Lipid peroxidation was determined in plasma as determined in material and methods section and indicated as MDA levels. The relationship of MDA levels (µM) levels in plasma related to T6MW, TUG, CST and HG tests are indicated. *Significant differences vs. respective low performance (p < 50) group, p > 0.05.

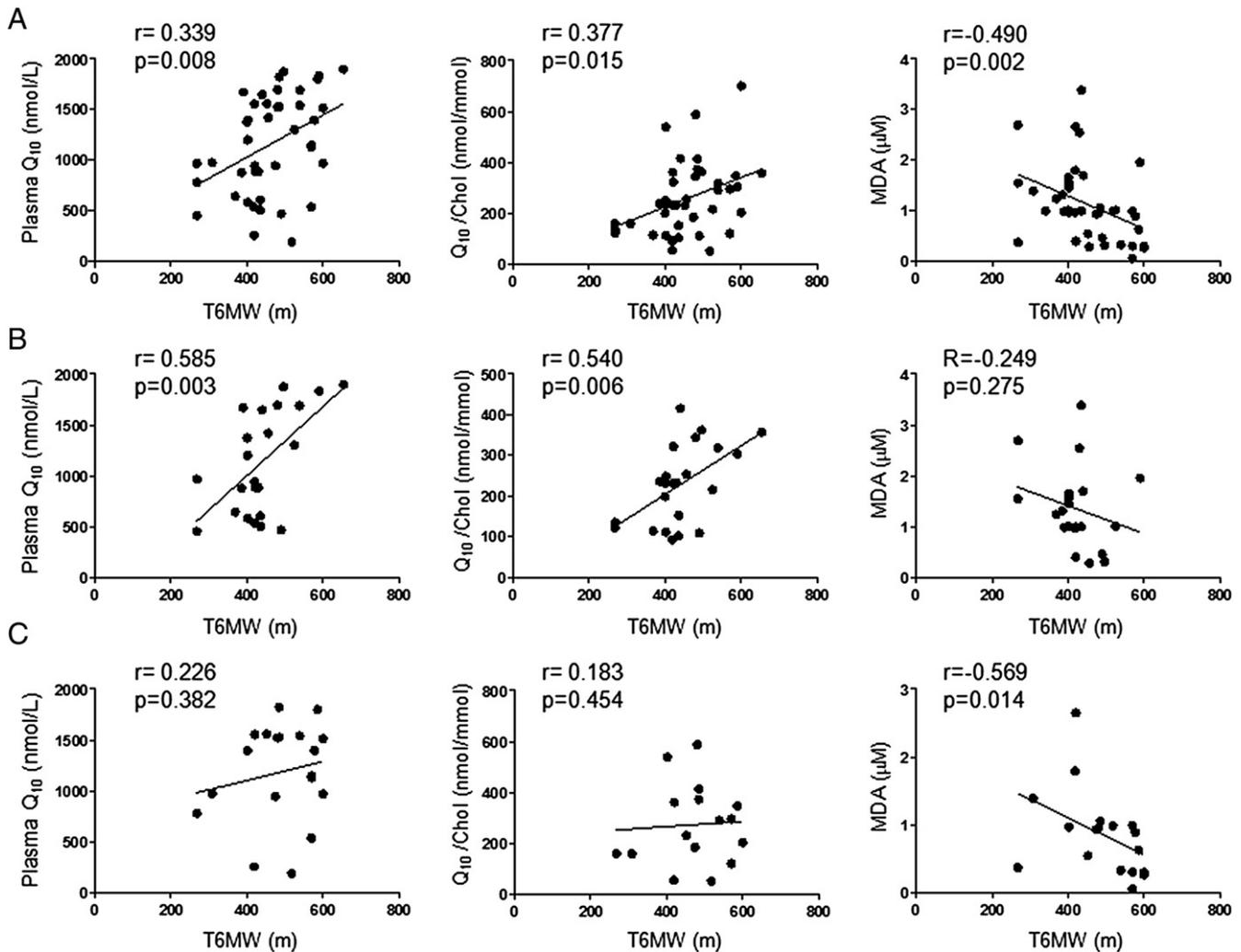


Fig. 2. Relationship of Q₁₀, Q₁₀/cholesterol and lipid peroxidation and cardiovascular fitness level. Levels of total Q₁₀ (left), relationship Q₁₀/cholesterol (medium) and lipid peroxidation measured as MDA levels (right) were related to the cardiovascular fitness measured by the 6 min walk test (T6MW) determined in meters. Correlations are divided in A) general population, B) women and C) men. Pearson r is indicated. Level of significance in each relationship is also indicated.

When we determined the correlation between total Q₁₀, Chol-C, LDL-C, Q₁₀/Chol, Q₁₀/LDL-C and MDA values and the BMI in both genders, we found that both men and women showed a negative high correlation between total Q₁₀/Chol-C plasma levels and BMI (Men: $r = -0.636$, $p = 0.036$; women: $r = -0.555$, $p = 0.009$). Additionally, a strong negative relationship between the BMI and total Q₁₀ ($r = -0.515$, $p = 0.017$) or Q₁₀/LDL-C ($r = -0.505$, $p = 0.019$) was detected in women. Moreover, MDA positively correlated with BMI in women and men ($p = 0.048$ and $p = 0.034$ respectively).

4. Discussion

Greater physical activity and functional capacity seem to lower ROS levels by inducing antioxidant mechanisms (Corbi et al., 2012), thus preventing several aging-related process diseases (Lee et al., 2012). Unfortunately, the association between oxidant/antioxidant markers and functional capacity has not been studied in depth in humans. We aimed to elucidate if there was a relationship between functional capacity and Q₁₀-related parameters and the levels of lipid peroxidation in human blood. The main finding of this study was that higher levels of functional capacity (mostly cardiovascular and strength capacity) were associated with higher levels of Q₁₀-related parameters in blood and with lower MDA values in blood of community-dwelling elderly people, hence supporting the notion that both aerobic and strength

exercise are necessary when prescribing exercise for the elderly (Martins et al., 2010).

Along with α -tocopherol, ascorbic acid, β -carotenes and glutathione, Q₁₀ is a non-enzymatic antioxidant (Knez et al., 2006; Urso and Clarkson, 2003). Within our elderly population, we found that larger levels of Q₁₀ associated with better levels of cardiovascular capacity, even when this parameter was normalized to the lipid profile or analyzed separately from men and women. Similarly, a further trend toward greater Q₁₀/cholesterol values was observed in those participants showing higher scores of strength. Although no studies have been conducted to determine the levels of plasma Q₁₀ in relation with functional capacity among elderly people, our results agree with other previous studies about physical activity levels and other antioxidant parameters (Aguilo et al., 2003, 2005; Rinaldi et al., 2006). It has been shown that treatment with Q₁₀ in healthy subjects does not increase exercise performance nor decrease oxidative stress (Bloomer et al., 2012), indicating that higher levels of Q₁₀ obtained from supplements do not produce higher physiological effect. However, in this same study, it was clearly stated that there is a positive relationship between physical performance and Q₁₀ levels in plasma, thus supporting our results and suggesting Q-dependent antioxidant effects of exercise.

Our results showing lower MDA values associated with better scores in cardiovascular capacity (Fig. 1) agree with previous works (Leelarungrayub et al., 2011) reporting that after 6 weeks

Table 4
Gender differences in biochemical variables based on fitness level (n = 43).

Variable	Fitness test						CST (no. of stands)						Hand grip dominant arm (kg)					
	T6MW (m)			TUG (s)			Men			Women			Men			Women		
	p < 50 (n = 7)	p ≥ 50 (n = 12)	Women (n = 11)	p < 50 (n = 10)	p ≥ 50 (n = 13)	Women (n = 11)	p < 50 (n = 11)	p ≥ 50 (n = 8)	Women (n = 8)	p < 50 (n = 12)	p ≥ 50 (n = 12)	Men (n = 9)	p < 50 (n = 10)	p ≥ 50 (n = 10)	Women (n = 11)	p < 50 (n = 13)	p ≥ 50 (n = 13)	
Q10 (nmol/l)	1065.06 (474.95)	1257.97 (495.72) ^a	949.86 (384.68)	1129.56 (497.64)	1250.61 (490.26)	1222.90 (493)	1205.48 (498.87)	1161.34 (496.)	1138.04 (498.68)	1124.75 (521.39)	1395.47 (347.94)	1062.19 (570.01)	1151.44 (471.85)	1114.44 (539.47)	1151.44 (471.85)	1114.44 (539.47)	1114.44 (539.47)	
Chol (mmol/l)	4.91 (1.34)	3.54 (1.54) ^b	5.39 (1.28)	3.89 (1.45)	4.21 (1.79)	5.65 (1.08)	3.79 (1.47)	4.39 (1.77)	5.28 (1.32)	4.85 (0.92)	4.23 (1.74)	3.87 (1.20)	4.78 (1.24)	5.28 (1.04)	4.78 (1.24)	5.28 (1.04)	5.28 (1.04)	
LDL-C (mmol/l)	5.43 (1.14)	4.11 (1.49) ^b	6.16 (1.42)	4.63 (1.45)	4.55 (1.62)	6.22 (1.07)	4.32 (1.35)	4.97 (1.68)	6.01 (1.58)	5.65 (0.99)	4.93 (1.77)	4.29 (1.20)	5.43 (1.50)	6.17 (1.05)	5.43 (1.50)	6.17 (1.05)	6.17 (1.05)	
Q10/Chol (nmol/mmol)	241.05 (160.64)	484.51 (373.10) ^b	178.12 (62.35)	383.82 (330.96)	407.02 (346.37)	232.90 (99.38)	428.68 (346.61)	348.23 (319.98)	218.79 (85.28)	235.30 (107.68)	418.32 (330.95)	373.65 (343.58)	243.87 (86.71)	212.81 (103.38)	243.87 (86.71)	212.81 (103.38)	212.81 (103.38)	
Q10/LDL-C (nmol/mmol)	197.98 (95.40)	360.64 (221.20) ^b	154.86 (52.59)	274.25 (173.42)	330.12 (230.31)	196.75 (77.29)	326.58 (218.31)	265.15 (175.54)	235.30 (107.68)	198.69 (84.39)	331.56 (220.91)	272.95 (183.52)	217.08 (77.91)	178.52 (80.31)	217.08 (77.91)	178.52 (80.31)	178.52 (80.31)	
MDA (µM)	1.23 (0.79) ^b	0.60 (0.37)	1.34 (0.57)	0.52 (0.35)	1.17 (0.69) ^b	1.14 (0.42)	1.01 (0.28) ^a	0.59 (0.46)	1.66 (0.91) ^a	1.01 (0.49)	0.69 (0.31)	1.00 (0.83)	1.04 (0.71)	1.58 (0.81)	1.04 (0.71)	1.58 (0.81)	1.58 (0.81)	

Q10: Coenzyme Q10 total levels; Chol: Total Cholesterol; LDL-C: low density lipoprotein; MDA: malondialdehyde; T6MW: six-minute walking test; TUG: Time up & go test; CST: Chair stand test; Hand Grip Dominant arm: Hand Grip test execute by dominant arm. a) p value < 0.05 for females in regard of the different fitness test; b) p value < 0.05 for males in regard of the different fitness tests.

of aerobic dance exercised intervention, MDA levels decreased significantly among previously sedentary women. Moreover, an inverse relationship between physical capacity and lipid peroxidation levels have been previously reported (Alessio et al., 1998; Davies et al., 1982; Duthie et al., 1990; Powers et al., 2011). Moreover, another study performed in men shows that after progressive resistance training, plasma concentration of MDA decreases (Azizbeigi et al., 2013). These results are also in line with the results shown in this manuscript, which indicate that those participants with higher scores on resistance strength, as measured by the CST test, also showed lower values of plasma concentrations of lipid peroxides. Since lower limb strength is closely related with agility in old people (Kwan et al., 2011), this statement would support the fact that better scores in the TUG test were also related with low levels of plasma MDA concentrations.

High BMI has been suggested to contribute to a poor health during the aging process (Gomez-Cabello et al., 2012), and exercise has largely been proposed as a treatment to reduce overweight and obesity (Warburton et al., 2006). However, the relationship of Q10 and obesity and health is currently matter of controversy. Different studies performed in adults indicate discrepancies in the relationship between BMI and Q10 showing similar, increased, or decreased Q levels in obese vs. nonobese individuals. In Miles' group work, a small increase in plasma Q10 levels was found in people showing metabolic syndrome (Miles et al., 2004b). However, in another study, people showing a BMI of around 54 did not show differences in Q10 levels compared to people with a BMI of 28.5 (Mancini et al., 2008).

However, biliopancreatic diversion reduced BMI and a drop of Q10 levels was found in the obese group, which reached even lower levels than the group showing lower BMI (Mancini et al., 2008). On the other hand, a positive correlation was found between platelets Q10 levels and BMI after treatment in people suffering anorexia nervosa, although no differences with normal population were reported (Niklowitz et al., 2012).

In agreement with our findings, Theuri et al., have recently shown that plasma Q10 levels are higher in Kenyan people living in the countryside and showing lower BMI than in Kenyan people living in the capital city, Nairobi, who as average show higher BMI (Theuri et al., 2013). In addition, Butler's group (Butler et al., 2003) showed a tendency for decreased plasma Q10 in obese patients. In another study, lower levels of Q10 were also found in adipose tissue from obese humans (Bour et al., 2011). It seems that Q10 levels are more sensitive to environmental or life habits than to the weight of the individual. It's likely that lower levels of Q10 in obese people are partly responsible for their higher levels of lipid peroxidation. These results agree with other studies showing higher oxidative stress related to obesity that can be reduced with exercise (Beltowski et al., 2000; Roberts et al., 2006). Data stratified by gender elucidate that our results were significant only in women, although a similar trend was found in men. The difference could be based on a strong, positive relationship between BMI and body-fat percentage found in women. One of the main findings of this study is the relationship between higher cardiovascular capacity and Q10 levels in plasma. In the circulation, Q10 is mainly carried out by lipoproteins, mostly in LDL particles (Bhagavan and Chopra, 2006).

Higher levels of Q10 in lipoproteins are directly related to LDL's higher resistance to initiation of lipid peroxidation (Mohr et al., 1992). Furthermore, Q10 has shown anti-atherogenic effects on apolipoprotein E knock-out mice models, indicating its effect against atherosclerosis (Witting et al., 2000). The positive cardiovascular effects of Q10 have been attributed to its capability to antagonize the oxidation of plasma low-density lipoproteins, and to its effect on ameliorating endothelial function (Belardinelli et al., 2006). There is also promising evidence of the beneficial effects of Q10 in the treatment of heart failure and hypertension (Pepe et al., 2007), and Q10 deficiency might be an important pathogenic mechanism involved in chronic heart failure (Littarru and

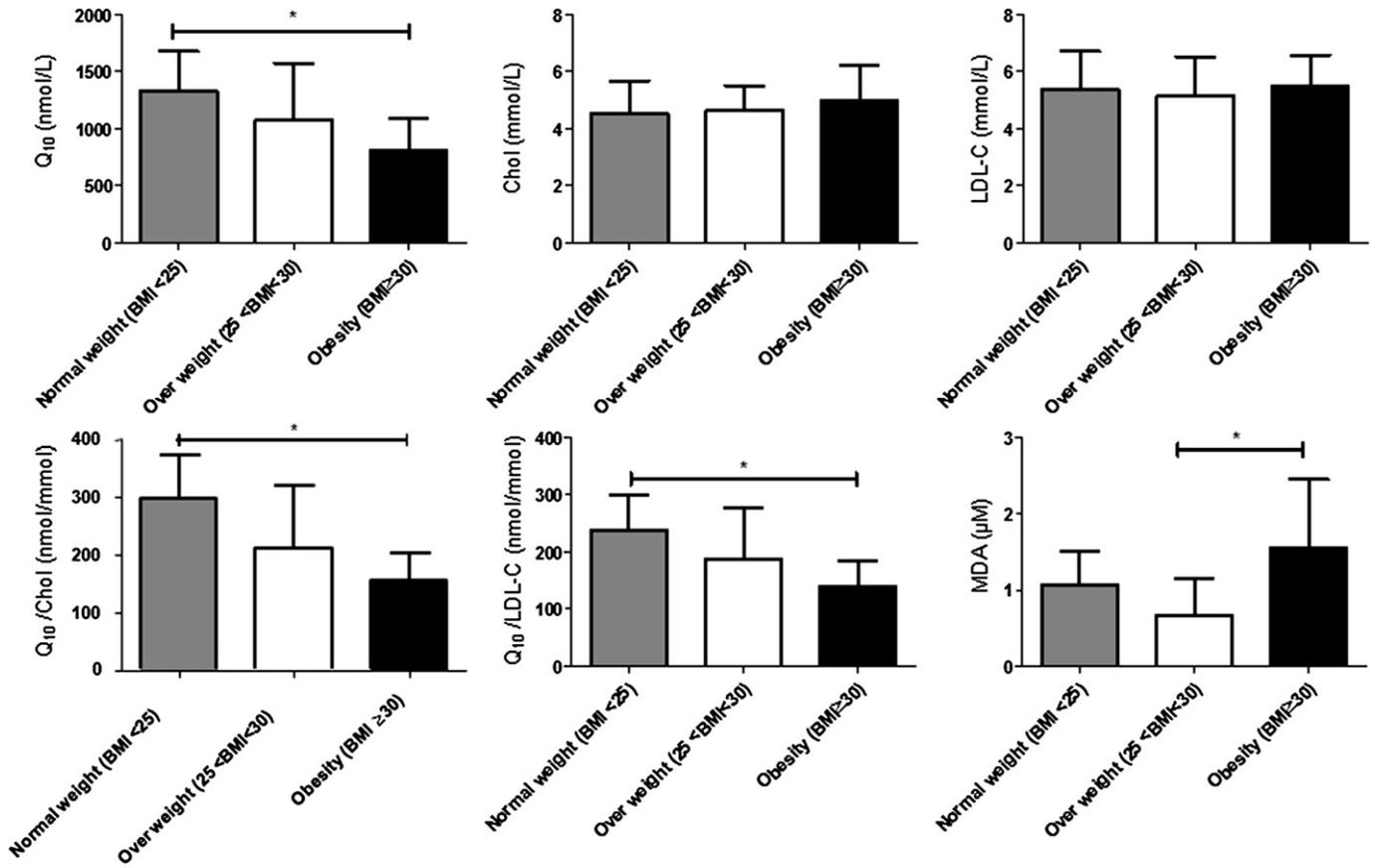


Fig. 3. Different in lipid profile, MDA and antioxidant status based on body mass index in general population of study. Plasma Q_{10} levels, cholesterol and Q_{10} relationship to cholesterol and LDL are indicated in relationship to the BMI of the general population including men and women. *Significant differences $p < 0.01$ or # $p < 0.05$.

Tiano, 2007). In fact, deficiency in plasma Q_{10} levels has been considered an independent predictor of mortality in patients suffering chronic heart failure (Molyneux et al., 2008). The increase of Q_{10} found in elderly people showing higher cardiovascular capacity indicates not only a

higher protection against oxidative stress, but a higher protection against cardiovascular diseases. It is then clear that increased physical activity improves cardiovascular capacity by increasing Q_{10} and $Q_{10}/LDL-C$ in plasma.

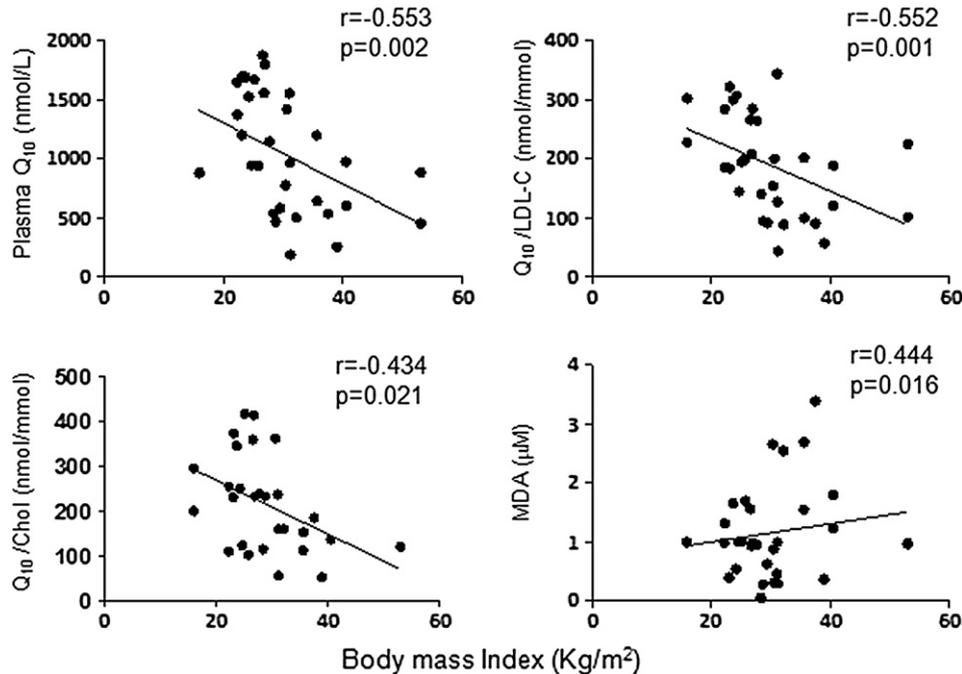


Fig. 4. Relationship between antioxidant status, oxidative stress and body mass index in general population. Plasma Q_{10} levels, $Q_{10}/Chol$, $Q_{10}/LDL-C$ and lipid peroxidation are correlated with the BMI index of the population. Pearson r is indicated. Level of significance in each relationship is also indicated.

Table 5
Gender differences in biochemical variables based on body mass index (n = 43).

Variable	Body mass index (kg/m ²)					
	Men			Women		
	Normal weight (n = 6)	Overweight (n = 6)	Obesity (n = 7)	Normal weight (n = 9)	Overweight (n = 7)	Obesity (n = 8)
Q ₁₀ (nmol/l)	1342.85 (346.09)	1251.56 (547.61)	910.12 (132.60)	1331.94 (363.01) ^a	1085.78 (676)	723.69 (264.20)
Chol (mmol/l)	4.95 (1.40)	4.55 (0.97)	4.37 (1.65)	4.87 (1.44)	5.06 (0.55)	4.97 (1.19)
LDL-C (mmol/l)	6.33 (1.26)	4.06 (1.5)	4.63 (0.45)	5.63 (1.73)	6.35 (1.00)	5.62 (1.16)
Q ₁₀ /Chol (nmol/mmol)	280.25 (79.88)	273.18 (164.71)	208.63 (86.19)	281.79 (71.49) ^a	209.18 (122.28)	149.91 (59.15)
Q ₁₀ /LDL-C (nmol/mmol)	219.87 (82.13)	316.77 (185.17)	196.75 (76.95)	244.38 (57.02) ^a	163.10 (85.20)	131.95 (52.45)
MDA (μM)	0.73 (0.27)	0.65 (0.43)	1.19 (0.83)	1.14 (0.45)	0.65 (0.61)	1.85 (0.90) ^a

CoQ₁₀: Coenzyme Q₁₀ total levels; Chol: Total Cholesterol; LDL-C: low density lipoprotein; MDA: malondialdehyde; a: p value < .05 for men and women regarding the body mass index.

To our knowledge, this is the first study analyzing the relationship between functional capacity, BMI and Q₁₀-related parameters or MDA plasma concentration among community-dwelling elderly people.

With our study, we try to identify evidence linking physical activity to reduction of factors associated with aging. Our work is focused on a population living in a narrow area where the most important differential factor is physical capacity of participants. We did not detect significant differences in nutrition or lifestyle.

This is important because many other studies have focused on working on populations differing in many factors, including lifestyle, environmental contamination, and availability of essential nutrients such as selenium for Q assembly in liver or liver damage (Tekle et al., 2010; Theuri et al., 2013). In conclusion, the results from our study suggest that a higher functional capacity (mostly cardiovascular and strength capacity) is associated with high levels of plasma Q₁₀ and related parameters and with low MDA values among community-dwelling elderly people. Moreover, lower levels of BMI accompany with low levels of MDA and high levels of Q₁₀-related parameters. Larger prospective cohort studies are required to confirm the relationships demonstrated in the current study. Longitudinal studies implementing programs designed to increase physical fitness (mainly cardiovascular capacity and muscle strength) will also clarify the relationships between the effects of such interventions on aging biomarkers.

5. Conclusions

Our study demonstrates for the first time that elderly people showing higher fitness also show better Q₁₀-dependent antioxidant protection in plasma. This higher protection is accompanied by a lower lipid peroxidation degree in plasma. To our knowledge, this is the first study that shows a relationship between fitness degree and Q₁₀ levels in plasma. We suggest that the practice of aerobic and strength exercise in elderly people can induce cardiovascular protection by increasing Q₁₀ and Q₁₀/cholesterol ratio in lipoproteins and decreasing oxidative stress. In practical terms, public health authorities should enhance the prescription of physical activity in aging-related programs to increase strength and cardiovascular capacity among community-dwelling elderly people.

Conflict of interest

All the authors declare no conflict of interest.

Acknowledgments

First, we want to thank the participants for their devotion and participation. The present study was supported by grants from the Government of Andalusia, Spain. The Centro Andaluz de Biología del Desarrollo

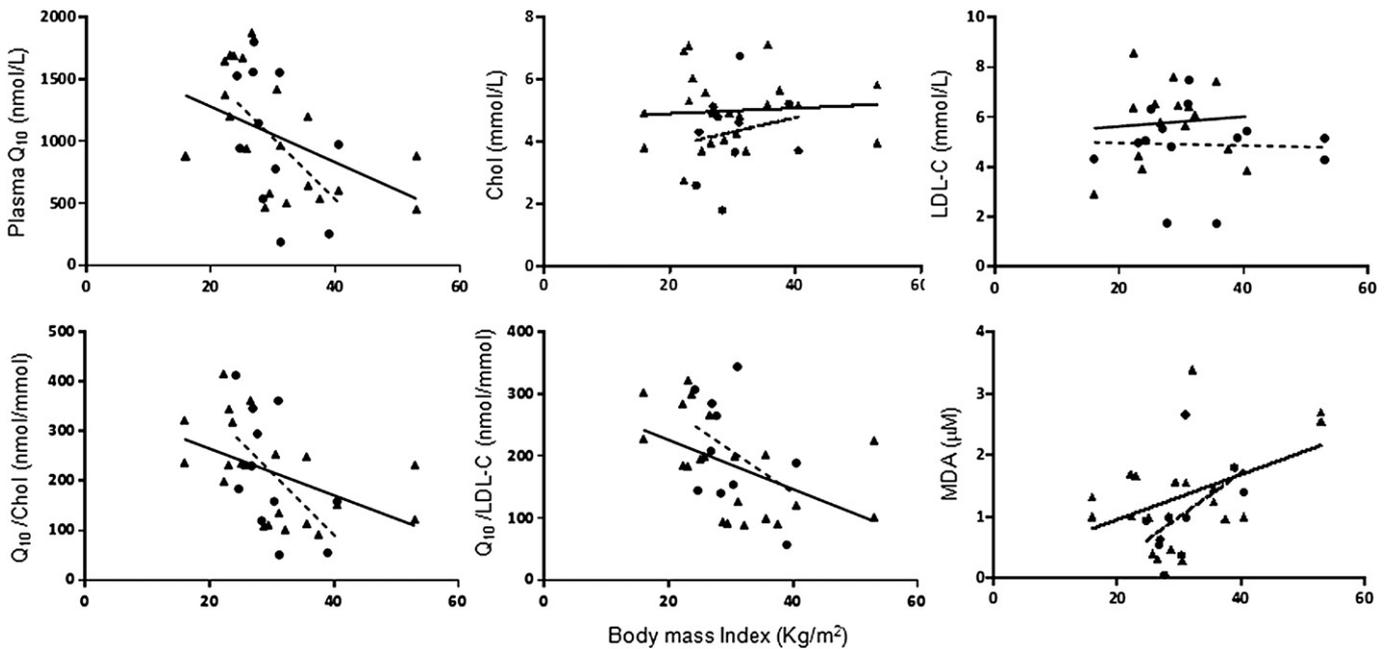


Fig. 5. Relationship of antioxidant status, lipid profile and oxidative stress and body fat and body mass index in men and women. Plasma parameters were correlated with the BMI index and separated depending on the gender of the population. Triangles and solid lines: women, circles and dashed lines: men. Pearson r and significance of the correlation are indicated in the text.

and Universidad Pablo de Olavide provided human and infrastructure resources funded by Andalusian Government by using FEDER funds (European Commission). Jesús del Pozo-Cruz was awarded a pre-doctoral fellowship funded by the project IMD2010-SC002 from the Centro Andaluz de Medicina del Deporte on behalf of the Government of Andalusia, Spain. We also thank the technical help of Estrella Gómez Bentoilla.

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