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Research on the protective effects of antioxidants on metabolic syndrome induced by thyroid dysfunction

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Abstract. – OBJECTIVE: This paper researches on the protective effects of antioxidants on metabolic syndrome induced by thyroid dysfunction. While the role of Lipoic acid (LA), Resveratrol (R) and Quercetin (Q) are recognized, the mechanisms for their am[illegible] tive effects are partially understood. The[illegible] the objective of this study was to determi[illegible]e prevalence of MS among university workers[illegible] to examine the relationship with thyroid fu[illegible] tion and mechanisms for prote[illegible] effects LA, Resveratrol and Quercetin[illegible]eart, kidneys and lungs.

SUBJECTS AND METHO[illegible] In the[illegible]ss-sectional study, a total of[illegible] univ[illegible]ers (1198 males and[illegible]107[illegible] age[illegible]60 participated. Anthropome[illegible]asurements (weight and hei[illegible] blood p[illegible]e, fasting plasma glucose[illegible] lipids, live[illegible] kidney function tests[illegible]re[illegible]ed out, thyroid stimulating hormon[illegible](TSH), [illegible]thyroxine (FT4), free triiodothy[illegible]ne (FT3), to[illegible]ioxidant capacity (T-AOC)[illegible]d peroxidation p[illegible]cts, malondialdehyd[illegible]DA), a[illegible]anced oxida[illegible]on protein products[illegible]OPP) [illegible]dityrosine levels were measu[illegible]

RE[illegible] furth[illegible]valuation of oxidative [illegible]ss i[illegible]s in[illegible]clinical hypothyroidism com[illegible]n normal thyroid function sho[illegible]d the[illegible]ences. Among middle-aged me[illegible]ith SCH (n = 467), MDA concentrations (8[illegible]ol/ml) were significantly higher [illegible]yroid[illegible]trols (7.34 ± 1.31 nmol/ml; n = 190) [illegible]ile AOPP, dityrosine and T-AOC levels were [illegible]different.

CONCLUSIONS: It was demonstrated that prev[illegible]ence of MS components was high. Targeting thyroid hormone restoration, inhibition of ACE and GSK3β via PI3K/AKT signaling path[illegible] using LA, [illegible]sveratrol and Quercetin are [illegible]ntial novel [illegible]apeutic approaches for de[illegible]ing pharm[illegible]uticals that could make significa[illegible]e in MS[illegible]atment.

Key Words:
Impact factor, Metabolic syndrome, Thyroid abnor[illegible] Numerical analysis algorithm.

Introduction

Non Communicable Diseases (NCDs) including cardiovascular diseases (CVDs), type 2 diabetes mellitus, chronic respiratory diseases and cancers are the leading causes of death worldwide. They account for almost 80% of global mortality, with 94 million of deaths occurring in low- and middle-income countries. China is emerging economies threaten by increasing rates of NCDs. WHO estimates that NCDs account for over 80% of total deaths, and for more than 70% of the country's health expenditures. Since the beginning of the 21st century, the country has made progress in prevention, but there are still large action gaps in implementation[1,2]. In the current National plan for Prevention and Treatment of NCDs (2012-2015), the main priorities are targeted towards prevention, timely detection and management of high-risk populations and promotion of healthy lifestyles[3]. However, the challenge is the prevalence of the main risk factor and the metabolic syndrome (MS) is varied across many regions of the country in rural-urban

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areas, among gender coupled with lack of awareness on existence of cardiovascular risks[4]. MS is almost becoming an epidemic, and is likely to overwhelm the health care systems and slow economic growth. Thus, targeting MS may be an important approach for the prevention, control and management of NCDs. Workplace environment is an important setting for health promotion and MS prevention since workers represent a large proportion of the total population. Work based health promotion programmers are effective in improving health related outcomes such as obesity, diabetes mellitus and cardiovascular disease risk factors. More specifically, work based health programs are an effective means of promoting a healthy diet and regular physical activity. Through the workplace, it is possible to influence health behaviors via multiple levels of influence; by direct efforts such as health education and increasing the availability of healthy foods and opportunities for physical activity; or indirectly through social support and social norms promoting healthy behaviors. However, the crucial basis for developing and implementing such interventions requires the determination of the major cardiovascular risk factors as well as their distribution patterns among workers in different occupations. The influence of occupation on cardiovascular risks is attributed to differences in work conditions such as shift work form and duration of work. Moreover, physical factors including noise and chemical exposure and psychosocial factors such as stress, lack of support, and socioeconomic status have effects on CVD risk. Such variations in work conditions lead to differences in cardiovascular disease prevalence, which suggests the need for workplace specific interventions. In China, extensive research on the MS prevalence has been carried out on the general population; however, information on workers is currently limited. Available reports demonstrate workplace related increase in MS prevalence among policemen and retired workers, while studies on university workers are few. Risk of factors such as heavy workload, sedentary long working hours, extended work schedules in Chinese universities, and differences conditions in comparison to the general population, the health status of university workers merits more attention. Workers are constantly exposed to work stress, which results in derangements in metabolic homeostasis mediated through indirect effects on health behaviors and direct effects on neuroendocrine stress pathways.

Acute or chronic stress has direct effects on hypothalamic- pituitary thyroid-adrenal axis (HPT) and the sympathetic nervous system resulting in clinical presentation of visceral obesity, diabetes, atherosclerosis and MS. Thyroid hormones are ended hormones of the HPT axis and are, therefore, altered in acute and repeated stress[5,6]. Despite the growing stress in university workers, there is paucity of data on the association of cardiovascular risks with thyroid function. Thyroid hormones, mainly the active triiodothyronine (T_3), exert significant effects on lipids, glucose and blood pressure resulting in elevated plasma levels and increased blood pressure and consequently, the risk. Furthermore, T_3 plays an important role in the regulation of mitochondrial function in several metabolically very active tissues such as skeletal muscle, heart, kidney, and liver. Thus alterations in levels lead to enhanced generation of reactive oxygen species (ROS) during metabolism resulting in overconsumption of non-enzymatic and enzymatic antioxidants[7]. This disturbs the pro-oxidant/antioxidant balance leading to oxidative stress and consequent damage to cellular structures, lipids, proteins, and DNA. Reduction of oxidative stress by prevention of ROS formation or by quenching of ROS using antioxidants has been used as an intervention approach in the past years. These strategies are reported to be effective in laboratory experiments while several clinical trials indicate that they do not reduce cardiovascular events, and in some cases antioxidants have worsened the outcomes. This may be caused by the antioxidants are not selectively taken up by mitochondria, but instead are dispersed throughout the body. Therefore, strategies for the targeted delivery of antioxidants to mitochondria are currently being developed. Mitochondria-targeted antioxidants developed as pharmaceuticals are shown to be effective and can be used in a wide range of human pathologies. These small molecules are developed from derivatives of antioxidants. Lipoic acid (LA) is a universal antioxidant known for its protective effects from chronic diseases associated with oxidative stress[8,9]. As an antioxidant, LA directly terminates free radicals, chelates transition metal ions (e.g., iron and copper), increases cytosolic glutathione and vitamin C levels and prevents toxicities associated with their loss. Moreover, polyphenols, occurring in fruit and vegetables, wine, tea, extra virgin olive oil, chocolate, and other cocoa products have been shown to exert beneficial effects on many

chronic diseases. Like LA, their biological effects are attributed to their antioxidant properties, either through their reducing capacities per se or through their possible influences on intracellular redox status. The ability to modulate the activity of various enzymes and thus interfere in signaling mechanisms in various cellular processes may be ascribed in part to their physiochemical properties that allow them to participate in different metabolic cellular oxidation-reduction reactions. Studies reporting the protecting effects of LA, Resveratrol and Quercetin on obesity and obesity-induced oxidative stress injuries on the heart, kidney and lungs have so far shown positive results however the mechanisms are not fully elucidated[10].

Subjects and Methods

Experiment 1: This was a cross-sectional study of 2428 University employees on annual clinical examination (November 2015-December 2015) at First Hospital in University. Some variables such as age, weight and height were missing in 155 participants hence were excluded in analysis. A total of 2273 participants were therefore evaluated (1198 males and females). The employees were further categorized into two occupational groups administration and academic workers. Administrators are involved with office work. They included the University top management staff, deans of schools and their assistants, departmental heads, top management staff from human resource, student affairs, graduate school, finance, procurement, medical, library, security and housing department. Academic workers are involved with research and teaching, and they included professors, associate professors, lecturers and laboratory technicians. All the study protocols were approved by University Ethical Committee and the Hospital Management. Informed consent was given by all participants. Study protocols were conducted in accordance with the Declaration of Helsinki recommendations of 1975, revised 2000.

Experiment 2: A random sample of 1150 adults (792 males and 358 females) aged between 30-60 years was obtained from the larger population sample (n=2428) for evaluation of thyroid function. The study protocols are explained which included the determination of anthropometric measurements, blood pressure, fasting plasma glucose (FPG), lipids and the diagnostic criteria for MS. Patients with diabetes mellitus, hyperthyroidism, sub-clinical hyperthyroidism, or individuals with history of thyroid disease or taking thyroxine or anti-thyroid drugs for treatment, or taking glucocorticosteroids, beta-blockers, amiodarone, antiepileptic drugs, salicylates, diuretics and other medications that affect thyroid function or taking lipid lowering drugs or with abnormal liver and kidney function tests were excluded from the study. Pregnant women or those within the first year post-partum period were also excluded from the study.

Data Collection, Physical Assessment, Blood Sample Collection and Preparation

Anthropometric measurements, weight (kg) and height (m) were measured using weight-height machine (RW-700, Zhengzhou, China) and used to compute body mass index (BMI). BMI ≥ 28 kg/m² was defined as obesity. Systolic and diastolic blood pressure was measured on the upper right arm using standard sphygmomanometer (YE-665 A, Jiangsu, China) after at least five minutes of rest. All measurements were taken by trained medical personnel. The overnight fasting blood samples were obtained in the morning by venipuncture and collected into sodium heparin vacationer tubes. Blood samples were kept on ice immediately, and plasma separated by centrifugation (KDC-1044, Hangzhou, China) at 1000 × g for 10 minutes at 4°C. Using standard biochemical reagents, an automatic Biochemical Analyser (HF 400, Shanghai, China) was used to measure enzymatically the levels of fasting plasma glucose (FPG), lipid profiles; triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), liver and kidney function tests[14]. All biochemical analyses were conducted in some content at the University hospital laboratory.

Definition of Metabolic Syndrome

Metabolic syndrome was defined according to the Modified criteria of the National Cholesterol Education Program Adult Treatment panel[15,16]. These criteria require the presence of at least three of the following five components: waist circumference ≥ 90 cm (males), ≥ 80 cm (females); systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or subjects treated with antihypertensive drugs; FPG ≥ 5.6 mmol/l; TG ≥

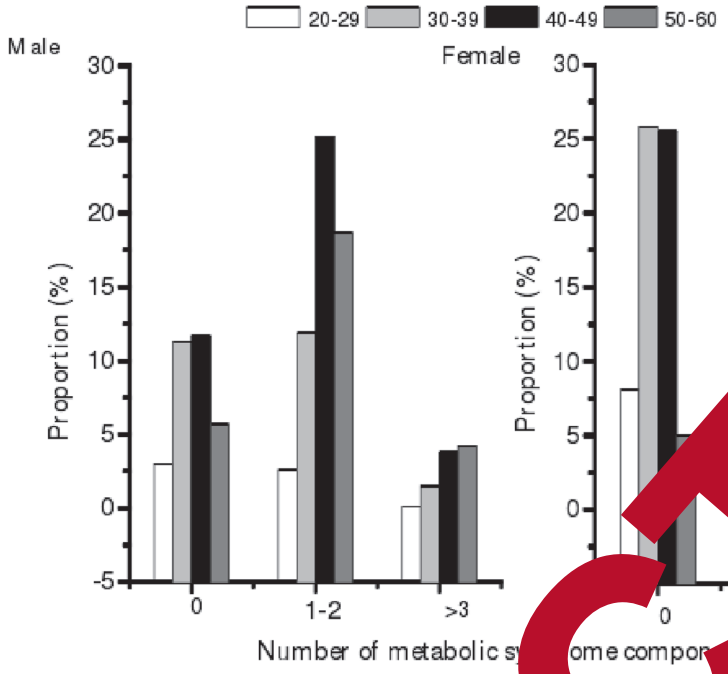

Figure 1. Sex-specific prevalence of the number of metabolic syndrome components by age groups.

1.695 mmol/l and HDL < 1.036 mmol/l (m
1.295 mmol/l (females). Plasma TSH, free t x-
ine (FT_4) and free triiodothyronine (FT_3) co
trations were determined by radioimmunoas
(xh6080, Xi'an) at Beijing Sino-u tute of Bi
logical Technology. The TSH vity was
0.5 mU/l; intra-and inter-as coeffici of vari-
ations of 0.5% and 10% ectivel
sensitivity was 0.16 pm l;
inter-assay coefficie vari respectively.
FT_4 assay sensiti was 0.15 p while in-
tra- and inter-as cients of va ns were
4.5% and 9.8% spec Normal thyroid func-
tion (euthy dism) was d as TSH level of
0.40-4.5 with normal F 9-25.60 pmol/l)
and F 20-9.2 pmol/l) level while subclinical
hyp roidis CH) was defined as TSH levels
of 4. th nor FT_4 and FT_3 levels.

Results

w ers were categorized into four age groups: 20-29, 30-39, 40-49 and 50-60 years old. Prevalence of MS components (hypertension, hyperglycemia, hypertriglyceridemia and low HDL varied across age groups in both males (χ^2 = 74.896, p = 0.001) and females (χ^2 = 53.587, p = 0.001). As shown (Figure 1), prevalence in the number of components was greater in 40-49 years age group among males (25.2%) and females (16.6%). Specifically, over a quarter (25.2%) of males and 16.6% of females aged between 40 and 49 years had at least one MS components. Table I shows the prevalence of MS and its components by sex. The overall prevalence MS was 6.1%, and was significantly higher (p < 0.01) in males (5.1%) than females (1.1%). The most prevalent compo-

Tab Prevale etabolic syndrome and its components by sex.

	All (n = 2273)	Male (n = 1198)	Female (n = 1075)	p
etabolic syndrome	139 (6.1)	115 (5.1)	24 (1.1)	0.001
igh body mass index	75 (4.0)	65 (3.5)	10 (0.5)	0.001
rtension	857 (37.9)	640 (28.3)	217 (9.6)	0.001
glycemia	294 (13.3)	234 (10.6)	60 (2.7)	0.001
Elevated triglycerides	462 (20.8)	357 (16.1)	105 (4.7)	0.001
Low HDL	307 (13.8)	137 (6.2)	170 (7.7)	0.001

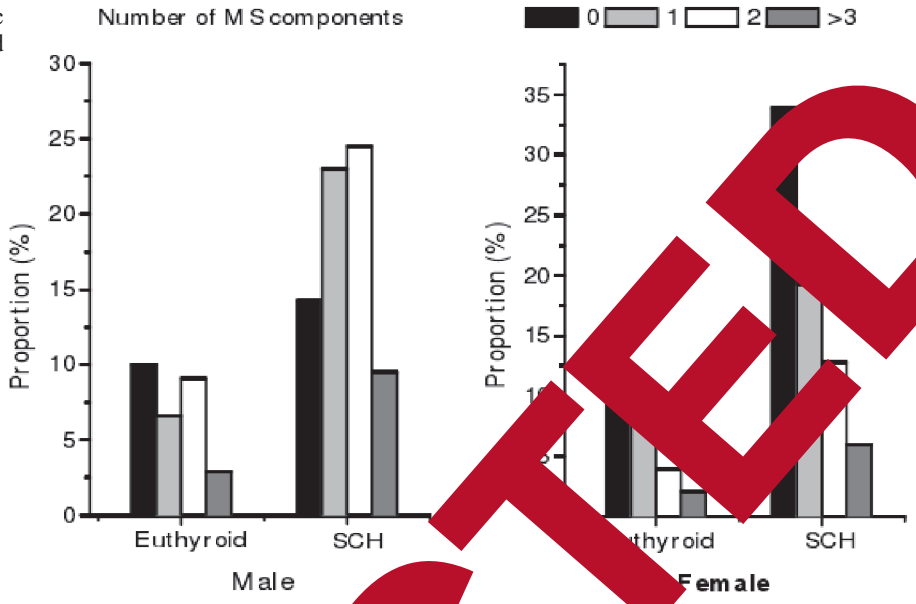

Figure 2. Prevalence of metabolic syndrome components by thyroid status.

nent in all participants was hypertension (37.9%), followed by elevated triglycerides (20.8%), low HDL (13.8%), hyperglycemia (13.3%), and obesity (4%). Male workers showed higher prevalence ($p < 0.01$) than females. Hypertension (2[illegible]%) and elevated TG (16.1%) were most freq[illegible] males while hypertension (9.6%) and low [illegible]L (7.7%) were common in females. Thyroid [illegible] tion of workers was evaluated to examine [illegible] possible association with lipi[illegible]cose an[illegible] blood pressure. Plasma TSH [illegible]ged be- tween 3.201 and 6.949 mI[illegible]nile F[illegible]nd FT_3 were within normal refe[illegible] level[illegible] pmol/l and < 9.20 pm[illegible]/l, [illegible]. Ba[illegible] TSH and levels of th[illegible]d hor[illegible] participants were categorized [illegible] two group[illegible]hyroidism SCH. As sh[illegible]n (Figure 2), there was a significant differen[illegible] ($\chi^2 = 20.013$, $p = 0.001$) in the n[illegible]r of MS [illegible]ponents in male adults with SCH [illegible] to those with normal thyroid functio[illegible] proportion of males with 2 MS components was 24.5% and 9.1% in the SCH and [illegible]id group, respectively. The corresponding [illegible]op[illegible]ons for the presence of 3 or more components were 9.5% and 2.9%. In females, there was no significant difference ($\chi^2 = 3.604$, $p = 0.307$) in the number of components between the two thyroid groups. Oxidative stress markers and T-AOC were compared between euthyroid and subclinical hypothyroid group (Figure 3). As illustrated, SCH group showed elevated MDA (8.11 ± 1.30 nmol/ml) levels than euthyroid controls

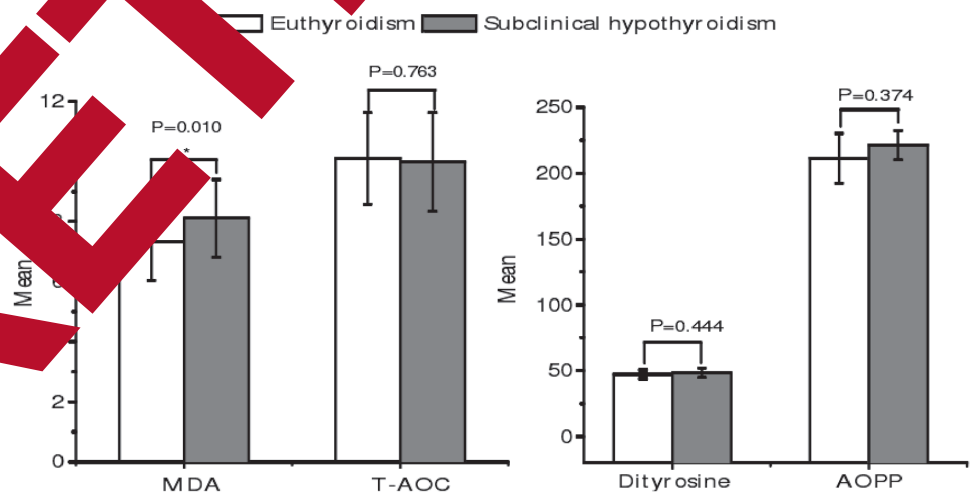

Figure 3. Oxidative stress markers in euthyroid and subclinical hypothyroid middle-aged men.

(7.34 ± 1.31 nmol/ml), whereas AOPP, dityrosine and T-AOC were not different ($p > 0.05$). The corresponding levels in euthyroids were; 211 ± 18.87 mmol/l, 47.08 ± 3.44 pg/ml and 10.10 ± 1.52 U/ml while levels in SCH were 221.39 ± 11.21 mmol/l, 48.27 ± 3.61pg/mol and 9.98 ± 1.64 U/ml, respectively. MDA levels were not associated ($p > 0.05$) with either TSH or thyroid hormones in SCH. After adjustment for age and BMI, TSH correlated positively (β = 0.186, $p = 0.034$) and inversely (β = -0.206, $p = 0.004$) with AOPP and dityrosine, respectively. AOPP correlated positively with FT_4 (β = 0.185, $p = 0.038$) while none of the oxidative stress markers associated with FT_3 and T-AOC. In the euthyroid group, dityrosine inversely correlated with FT_4 (β = -0.397, $p = 0.015$) after age and BMI adjustment while it correlated with FT_3 (β = -0.324, $p = 0.017$) when only age was adjusted. Moreover, T-AOC reduced (β = -0.327, $p = 0.030$) with increased MDA. The mice fed with HFD consistently gained more weight than controls, and was markedly increased ($p < 0.05$) by 6th week (Figure 4 A-B). Supplementation with LA (22.60 ± 0.73 g) reduced weight to control levels (22.38 ± 0.46 week whereas Resveratrol and Quer mhib ed weight gain at the end of feedin 26 weeks, body weight reduced in HFD +L 42 ± 0.25 g), HFD + R (29.18 ± 0.75 g) nd HF (29.13 ± 0.69 g) compared with (35.40 g) mice, and higher than c ols (26.47 ± As compared to contr nd ant ant gro the HFD mice had s anth < 0.05) higher systolic blood pre re d diast blood pressure (DBP) th week re 4). However, the SB 619 ± 3.522 and DBP (64.635 ± Hg) of HFD ce increased at 24 we comp to controls (SBP, 79.724 ± 6.239 mmHg; DB 058 ± 3.819 mmHg) wh ntioxidants re d blood pressure to n al levels. Similarly, the heart pulse rate of D mice (698. ± 42.58 beats per minute) was

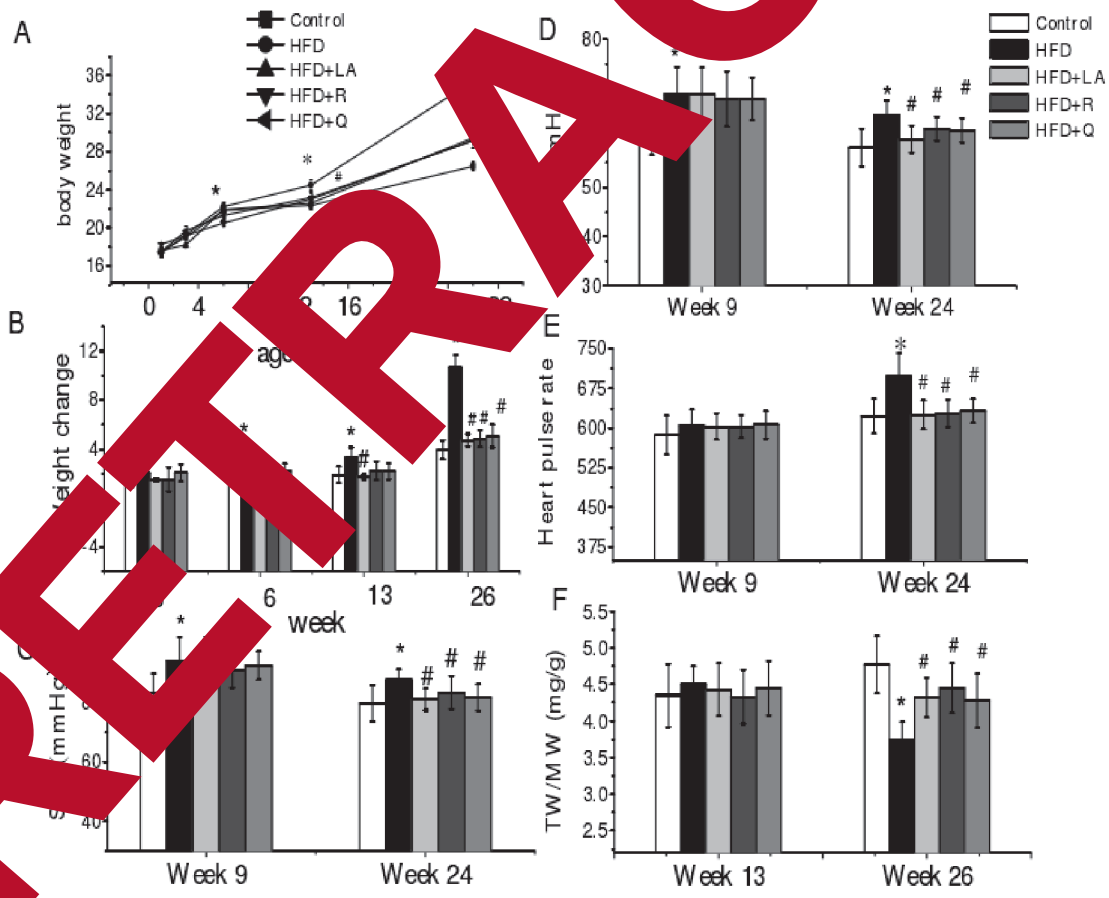

Figure 4. Changes in physiological parameters of mice over the experimental period. Plots are shown for body weight in grams ***(A)***, weight change ***(B)***, SBP-systolic blood pressure ***(C)***, DBP-diastolic blood pressure ***(D)***, heart pulse rate in beats per minute ***(E)*** and TW/MW-tissue weight/body weight ***(F)***.

higher ($p < 0.01$) than controls (622.71 ± 32.84 beats per minute) at 24 weeks while the rate was reduced by all antioxidants. The TW/MW ratio reduced significantly ($p < 0.01$) in HFD mice (3.75 ± 0.24 mg/g) compared to controls (4.77 ± 0.39 mg/g) at 26 weeks and was improved with antioxidant supplementation (Figure 4F). The ACE activity in HFD mice (0.755 ± 0.435 U/mg protein), HFD +LA (0.146 ± 0.048 U/mg protein), HFD + R (0.216 ± 0.08 U/mg protein) and HFD + Q (0.162 ± 0.035 U/mg protein) were significantly lower ($p < 0.01$) than controls (1.474 ± 0.199 Umg/protein) at 13 weeks (Figure 5 A). However, by 26th week, the activity increased ($p < 0.05$) in HFD mice (0.69 ± 0.225 U/mg protein) compared to controls (0.28 ± 0.114 U/mg protein) while reduced in HFD + LA (0.231± 0.02 U/mg protein) and HFD + Q (0.182 ± 0.096 U/mg protein) mice. Moreover, compared to controls (5.760 ± 1.838 U/mg protein), the activity of NOS significantly increased ($p < 0.01$) in HFD mice (9.450 ± 1.004 U/mg protein) at week 13 and reduced in HFD + LA (4.367 ± 0.569 U/mg protein), HFD + R (4.456 ± 1.971 U/mg protein) and HFD + Q mice (3.091 ± 0.818 U/mg protein) (Figure 5B). Conversely, the activity reduced ($p < 0.01$) in HFD mice (3.19 ± 0.656 U/mg protein) compared to controls (10.19 ± 2.155 U/mg protein) at the end of feeding. while HFD + R (10.466 ± 2.798 U/mg protein) increased activity to control levels. Furthermore, the activity of Ca^{2+}-ATPase was significantly higher ($p < 0.01$) in HFD mice (12.73 mg protein) than controls (7.75 ± 1.6 mg protein) at 26 weeks while reduced to control levels in HFD + LA (6.20 ± 1.57 U/mg protein), HFD + R (6.68 ± 1.60 U/mg protein) and HFD + Q mice (5.77 ± 1.63 U/mg protein) at 13 weeks. Na^+/K^+-ATPase activity was lower ($p < 0.01$) in HFD mice (5.262 ± 1.455 U/mg protein) compared to controls (10.472 ± 1 U/mg protein), HFD + LA (8.162± 1.084 mg protein), HFD + R (9.632 ±1.337 U/mg protein) and HFD + Q (9 ± 1.099 U/mg protein). However, the activity increased significantly ($p < 0.01$) in HFD mice (14.93 ± 2.48 U/mg protein) at 26 weeks than in controls (8.00 ± 0.28 U/mg protein). reduced with antioxidant supplementation to control levels (Figure 5 C). The enzyme activities of HFD + LA, HFD + and HFD + mice were 8.50 ± 0.14 U/mg protein, 8.98 ± 1 U/mg protein, 7.27 ± 2.35 U/mg protein, respectively. The relative changes in the thyroid hormone receptor gene (TRα1), iodothyronine type I (DIO1) and redox sensitive genes are shown in Figure 6. weeks, the HFD mice had a 1.5-fold ($p < 0.05$) in TRα1 expression compared

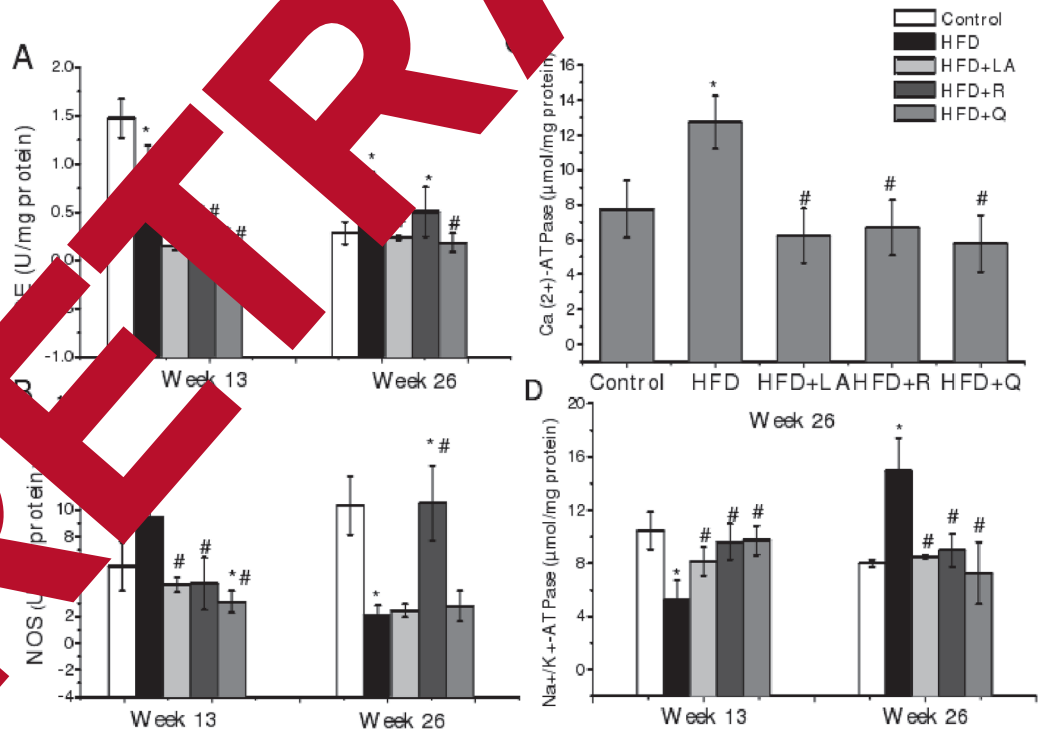

Figure 5. Effect of diet on enzyme activity of ACE, NOS, Na+/K+-ATPase and Ca (2+)-ATPase in the heart.

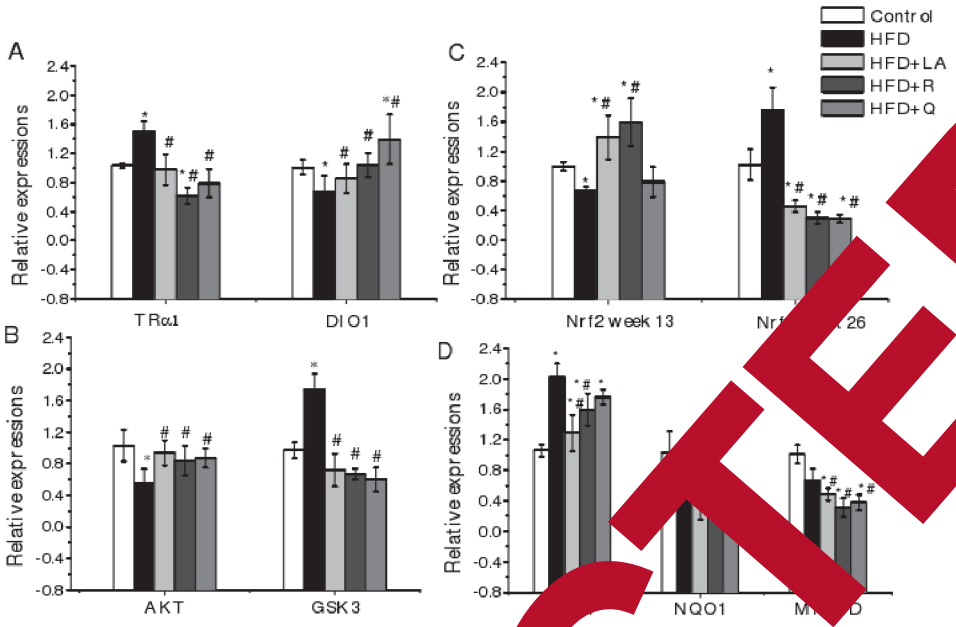

Figure 6. Expression changes of TRα1, DIO1, Akt, GSK3β, M[illegible]D, Nrf2 and i[illegible]rget genes in the heart.

to controls and antioxidant groups, whereas DIO1 expression declined (Figure 6 A). Additio[illegible]y the mRNA levels of Akt were lower ($p <$ [illegible] HFD group while GSK3β increased 1.7 fold [illegible]n-pared to control mice (Figure 6 B). Antioxid[illegible] increased ($p < 0.05$) the expression of Akt [illegible] reduced GSK3β expression. In [illegible]he expre[illegible] sion of Nrf2 and its target g[illegible]ncreased 1.8 and 2- fold respectively[illegible]pared [illegible]controls while expression in anti[illegible]nt mic[illegible]wer (Figure 6 C, D). The [illegible] and NQO1 were low[illegible] HFD [illegible]compared to controls. Levels [illegible]nSOD in a[illegible]dant mice were lower than [illegible]ile NQO1ex[illegible]ion was not different ([illegible] 0.05).

Discussion

O[illegible]ti[illegible]as obs[illegible]d to influence cardiovascula[illegible] as re[illegible]ed in other workplace. adju[illegible]t [illegible]age, administrative work ass[illegible]ted wi[illegible]reased prevalence of hypertens[illegible] and hyp[illegible]glycemia in male workers, and h[illegible] females. However, administrative female[illegible]showed lower prevalence of hyper[illegible]lyceridemia as compared with those in academ[illegible]s. Prevalence of obesity, low HDL and MS was[illegible]t different between the two occupations in both sexes. In addition, there was no association between professional position and cardiovascular risk[illegible] workers. The difference in cardiova[illegible] risks in administrative and academic work is ascribed to nature of work in the [illegible]upation groups. Administrative or office [illegible]volves sedentary behavior characterized by too much sitting while academic work requires movements to lecture buildings. Too much acute and chronic uninterrupted sitting is associated with cardiovascular risks independently of physical activity due to low energy expenditure, reduced insulin action and reduced skeletal muscle lipoprotein lipase activity. Lipoprotein lipase is a key enzyme for fatty acid and lipoprotein metabolism in muscle. A decrease in its activity results in reduced uptake of TG and glucose. In this regard, sedentary behaviors could potentially be targeted independently from physical activity and dietary intake interventions to reduce MS in the workplace. Current interest is on determinants of cardio metabolic risks in workplace to facilitate health interventions that help reduce rising medical costs. Interventions such as stretch-break programs and use of sit-stand devices reduce sitting time and generate health benefits. The study showed marked heterogeneity in metabolic alterations by gender, occupation and thyroid function. In the study, the dyslipidemia pattern, increased blood pressure, and hyperglycemia observed in male workers compared to females is attributed to the action of thyroid hormones. The active thyroid hormone, T3 has significant effects

on lipids, carbohydrates and on the cardiovascular system. Notably, FT_4 and FT_3 levels were significantly higher in males than females despite similar levels of TSH. It is possible that TSH stimulated increased production of T4, which in turn was activated to T3 since the FT_3/FT_4 ratio was also increased in males. T3 affects the synthesis, mobilization and degradation of lipids, although degradation is influenced more than synthesis. Thus, increased levels stimulate fat mobilization, leading to increased concentrations of fatty acids in the plasma. T3 can also stimulate hepatic glucose production via direct actions on the liver or indirectly via a sympathetic pathway from the hypothalamus. The T3 mediated effects on the systemic vasculature include relaxation of vascular smooth muscle resulting in decreased arterial resistance and diastolic blood pressure. Thus, in hyperthyroidism, cardiac contractility and cardiac output are enhanced and systemic vascular resistance is decreased, while in hypothyroidism, the opposite is true. Oxidative stress plays a role in the pathogenesis of many chronic diseases including CVDs. Prospective studies indicate that patients with SCH have incr d risks for all-cause and cardiovascular m and thus presence of oxidative stress in the a- tients could further enhance risks. In this s oxidative stress was found to be increased in S due to elevated plasma lipids ind y low th roid function. The SCH grou dyslip- idemia pattern compared t yroid trols at- tributed to increased bod ght. Ob ts thyroid function via m y n s lin increasing levels of in ho which sub- sequently affects production ptin stim- ulates the hyp s-pituitary- d axis, regulates the roid tor gene expression, and is inv d in the ac on of T4 to T3 by deiodina zyme. Thus, it sible that leptin cause ild ele ation in TSH, which stimulated the oid t crease production of T4 and secr of T3 in affected lipids by in- creasin xpressi genes for key enzymes ed i olism.

Conclusions

Supplementation with antioxidants inhibited t gain and reduced oxidative stress, which led improvements in endothelial function, reduction in blood pressure, heart pulse rate, cardiac hypertrophy and fibrosis. Antioxidants ameliorated oxidative stress by attenuating ROS, increasing GSH levels and catalase activity, improving antioxidant capacity; by restoring T3 levels via reducing expression of TRα1and increasing pression; by inhibiting ACE and AT pressi with subsequent reduction in Ang sin II activation; by improving Ca^{2+} handl reducing the expression of Na^+/ATPase gene (1), and by inhibiting GSK3β via PI kt signa th way. Collectively, LA, R ratrol and Qu are cardio protective their a y to res thyroid hormone lev hibit E activity and the expression of TP GSK3β cates their novel ther ic pote

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uthors declar they have no conflict of interests.

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