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Long-term effects of an exercise and Mediterranean diet intervention in the vascular function of an older, healthy population

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ABSTRACT

Background: Preserving endothelial function and microvascular integrity is suggested to reduce cardiovascular disease risk. It was recently shown that the age-dependent decline in endothelial and microvascular integrity may be reversed when combining exercise with Mediterranean diet (MD) in an 8-week intervention. The present study investigates whether the risk-reduction improvement in microcirculatory and cardiorespiratory functions are sustained in this age-group after a 1-year follow-up.
Design and methods: Twenty sedentary healthy participants (age, 55 ± 4 years) from the original study underwent cardiopulmonary exercise tolerance test and were assessed for their upper- and lower-limb vascular endothelial cutaneous vascular conductance (CVC) using laser Doppler fluximetry (LDF) with endothelium-dependent [ACh (acetylcholine chloride)] and endothelium-independent [SNP (sodium nitroprusside)] vasodilation, 1 year after completing the intervention.
Results: Both MD and exercise groups appeared to have an improved microvascular responses, in comparison to baseline as far as ACh is concerned. Exploring the interactions between the time point and the original group, however, revealed a stronger improvement in the MD group in comparison to the exercise group, for ACh ($p = 0.04$, $d = 0.41$). In the upper body, the time point and group interaction for ACh, indicated a better improvement for MD, without however statistical significance ($p = 0.07$, $d = 0.24$). Additionally, cardiorespiratory improvement in ventilatory threshold was maintained, 1 year after (12.2 ± 3.0 vs. 13.2 ± 3.2 ml · kg^{-1} · min^{-1}, $p < 0.05$).
Conclusions: The original improvements from an 8-week exercise and MD intervention were still evident, particularly in the microcirculatory and cardiorespiratory assessments, 1 year after the initial study. This suggests that a brief intervention combining MD with exercise in this high-risk group promises long-term health benefits.

Introduction

Maintaining microvascular integrity is a crucial element of our health and well-being and is affected by the ageing process (Gates et al., 2009). A healthy microcirculatory system cannot only affect tissue viability and susceptibility but could potentially play a predictive role in disease generation and progression (Kahaleh, 2008; Khan et al., 2010; Klonizakis et al., 2003).

The relationship between the attenuation of skin microvascular, vasodilatory responses and ageing alone is well documented (Gates et al., 2009; Tew et al., 2010), being largely the result of a depleted endothelial function (Gates et al., 2009). A number of studies (i.e., Dod et al., 2010; Versari et al., 2009) have exemplified the importance of maintaining endothelial function unaltered, as endothelium appears to be an early and important promoter for atherosclerosis and thrombosis, playing a decisive role in the occurrence of cardiovascular events.

With the occurrence of cardiovascular disease being on the rise (OECD, 2013) and subsequently the disease management cost adding a huge burden to healthcare systems around the globe (i.e., more than £28 billion in the UK alone; Luengo-Fernández et al., 2006), it is important to find appropriate strategies to stimulate disease reduction. It seems to be a poignant time to invest in strategies that reduce the risk of cardiovascular risk within a growing population of middle- to older-aged people in the Western world and in the UK in specific (ONS, 2012).

An emerging body of evidence suggests moderate-to-vigorous physical activity can reduce the risk of many chronic conditions, including cardiovascular diseases [Hamer and Stamatakis, 2009; Klonizakis et al., 2012; Warburton et al., 2006). Exercise, however, can only respond partially to the problem as it is widely agreed that our health is the result of a continuous interaction between a host of potential influences (Barton

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and Grant, 2006; Marmot et al., 2012), including (but not limited too) genetic, environmental and social factors. Although exercise on its own can beneficial, other lifestyle factors such as nutrition can play an important role as well, positively affecting our physical well-being throughout life (Kumanyika, 2012).

A number of healthy diets have been recently proposed to benefit health, including the Japanese (Willcox and Willcox, 2014), Nordic (Mithril et al., 2012) and Mediterranean (Bach-Faig et al., 2011) diets. The Mediterranean diet [MD] has being particularly highlighted for its purported positive cardiac health effects and the potential to reduce chronic disease development (Estruch et al., 2013). Adherence to the MD [which is based on olive oil, fruit, vegetables and salad, fish, legumes, wholegrain foods, wine and limited consumption of red meat] has been associated with a significant improvement in health status as seen by a reduction in overall mortality and deaths due to cardiovascular causes; 9% for both (Sofi et al., 2008).

Considering the scientific evidence, it makes sense to attempt and promote the combined consumption of a healthy diet that has been proven to provide cardiovascular effects with exercise, focusing in the small veins of our body, due to their important role in our overall well-being. With the number of studies attempting this being limited (i.e., Lucas et al., 1987; Montero et al., 2012), it was recently attempted to bridge the knowledge gap, investigating the medium-term effects of an intervention that combined a lower-limb exercise training [in the form of treadmill-based exercise] and the MD, on both lower- and upper-limb cutaneous microvascular functions in a healthy, older population (Klonizakis et al., 2012). The original study attempted to create equilibrium between internal and external validity with a pragmatic approach. First, we avoided implementing strict and full adherence to the MD, opting for a flexible educational and motivational method to promote consumption of the MD in a small sample of middle- to older-aged adults who resided in the UK. This age-group had little experience with this type of eating pattern and had no cultural or traditional connection to such a diet. Thus, we anticipated any strict adherence protocol as a challenging prospect for the participants. Hence, we implemented individual advisory and tailored sessions to prepare the participants to change current dietary habits. During those sessions, we encouraged the increase in several items of food and drink, which are strongly associated with beneficial health effects (vegetables, fruits, olive oil, tree nuts and fresh oily fish). When combining exercise with MD, we relied on allowing the participants to select from a range of effective intensities within the mild-to-moderate-intensity domains, which allowed an excellent (approximately 90%) compliance throughout the 8 weeks in both MD and non-MD groups. This pragmatic approach resulted in short-term effectiveness in reversing the age-dependent decline in exercise tolerance and improving microcirculatory endothelial function, especially in the MD group (which combined MD and exercise) (Klonizakis et al., 2012). However, the longer-term compliance that is needed, in order to sustain these cardiovascular risk-reduction benefits, is unknown.

This investigation follows up from the original data recorded for lower- and upper- limb cutaneous microvascular and cardiorespiratory assessments 1 year after the end of the original study (Klonizakis et al., 2012). The aim of this study was to examine if the participants retained any of the original microcirculatory and cardiovascular benefits in this time frame.

Methods

Twenty out of 22 participants of the original study (2 dropped out due to relocation) returned for this follow-up study after 1 year since they completed the original intervention. Since then, participants received no instruction or support regarding exercise and/or the MD. The consumption of MD was not reported by any of the participants in either groups at the time of the follow-up measurements.

No reason for exclusion existed for any other of the original cohort, and there was no change in participants' health status (Table 1). None of the participants was smoking or receiving β-blockers at the time of their follow-up assessment. Participants were asked to refrain from any regular or structured exercise activities for 48 h and to abstain from caffeine for 24 h prior to the measurement session. This study gained institutional ethical approval and was carried out in accordance with the Declaration of Helsinki of the World Medical Association.

Assessment of cutaneous microvascular function

All microvascular assessments were performed in a temperature-controlled room [range, 22–24 °C] following a 10-min acclimatization period.

Laser Doppler fluximetry measurements [moorVMS-LDF2, Moor Instruments] involved an incremental dose–response iontophoresis protocol (Klonizakis et al., 2012) using two Perpex probes with 80 μl of the endothelium-dependent ACh [Miochol-E; Novartis] and endothelium-independent SNP [sodium nitroprusside; Rottapharm, S.L.] vasodilators. All participants were assessed for both lower and uppers body in supine position as previously described (Klonizakis et al., 2003, 2012).

Cardiopulmonary exercise assessment

Following a 15-min rest, participants followed an incremental exercise test on a treadmill [Cosmos HP Mercury 5.0, Nussdorf-Traunstein / Germany] with velocity initiated at 2.0 km/h and was increased by 1.0 km/h every 3 min until reaching the test termination criteria as previously stated (Balady et al., 2010). Cardiopulmonary responses of $\dot{V}O_2$ [oxygen uptake], $\dot{V}CO_2$ [CO_2 production] and RER [respiratory exchange ratio] were continuously measured breath by breath, using an online gas analyser [Metalyzer Cortex 3B]. Flow sensor and gas analysers using gases of known concentration [16% for O_2 and 5% for CO_2] and a 3 L gas volume syringe were calibrated prior to each test.

Data recording and analysis

Microvascular, endothelium-dependent and endothelium-independent functions were measured via peak cutaneous flux responses to ACh and SNP, recorded in conventional PU (perfusion units) (Klonizakis et al., 2012). T_{max} (time to reach maximum perfusion) was also measured (Klonizakis et al., 2011).

Cutaneous blood flux data were also divided by mean arterial pressure to calculate cutaneous vascular conductance (CVC). Differences in group characteristics were assessed using independent Student's *t* tests and χ^2 tests. Mixed-model (group by time) analysis of co-variance (ANCOVA) was used to detect changes in outcome measures between groups, with baseline data used as the covariate. Effect sizes (Cohen's *d*) were calculated for the exercise group data, with 0.2, 0.5 and 0.8 representing small, medium and large effects, respectively. Cardiorespiratory $\dot{V}O_2$ and $\dot{V}CO_2$ data were averaged for the final minute of each stage, while ventilatory threshold (VT) was determined

Table 1
Demographics of participants.
Values are presented as means ± SD.

Variable	Exercise group	Mediterranean diet group	*p* value
Gender (*n*) (female/male)	7/3	7/3	1.00
Age (year)	57 ± 4	56 ± 4	0.85
Body mass (kg)	75.2 ± 17.3	76.9 ± 13.9	0.44
Stature (cm)	165.8 ± 9.9	167.4 ± 7.7	0.88
MAP (mean arterial pressure) (mmHg)	96.1 ± 14.4	94.6 ± 12.5	0.61
Systolic pressure (mmHg)	124.4 ± 21.5	125.5 ± 11.0	0.69
Diastolic pressure (mmHg)	79.3 ± 10.5	77.5 ± 10.9	0.61
Regular Exercise (yes/no)	7/3	5/5	0.39