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Original article

Monounsaturated fatty acids might be key factors in the Mediterranean diet that suppress rheumatoid arthritis disease activity: The TOMORROW study

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SUMMARY

Background & aims: The Mediterranean diet is reportedly effective in suppressing disease activity in rheumatoid arthritis (RA), but the key elements responsible for this effect remain unknown. The presented study therefore aimed to identify such elements.

Methods: This study included 208 consecutive patients with RA (RA group) and 205 age- and sex-matched healthy volunteers (controls) from the prospective "TOMORROW" cohort study that has been ongoing since 2010 were included in this study. Food and nutrient intake was assessed using the brief self-administered diet history questionnaire (BDHQ), Mediterranean diet scores were calculated based on intake by controls and disease activity was determined from disease activity scores in 28 joints and erythrocyte sedimentation rates (DAS28−ESR).

Results: Intake of monounsaturated fatty acids (MUFA) was significantly lower in the RA, than in the control group ($P = 0.003$) and the ratio of consumed monounsaturated to saturated fatty acid (MUFA/SFA) significantly differed within the RA group after being sub-classified according to DAS28−ESR. Moreover, DAS28−ESR significantly correlated with MUFA/SFA intake after age adjustment ($R = -0.228$, $P < 0.01$). Logistic regression analysis selected high MUFA intake as an independent predictor of remission in the RA group with borderline boundary significance (odds ratio, 1.97; 95% CI, 0.98−3.98; $P = 0.057$). Changes in DAS28−ESR between 2010 and 2011 significantly correlated with MUFA/SFA intake after age adjustment ($R = 0.180$, $P = 0.01$).

Conclusions: Daily MUFA intake, a component of the Mediterranean diet score, might suppress disease activity in RA patients.

Abbreviations: BDHQ, brief self-administered diet history questionnaire; bDMARD, biological disease-modifying antirheumatic drugs; C, control; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; DAS28−ESR, disease activity score in 28 joints−erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drugs; EULAR, European League Against Rheumatism; HDA, high disease activity; LDA, low disease activity; MDA, moderate disease activity; mHAQ, modified health assessment questionnaire; MUFA/SFA, monounsaturated fatty acid to saturated fatty acid ratio; PSL, prednisolone; RA, rheumatoid arthritis; SJC, swollen joint counts; TJC, tender joint counts; VAS, visual analog scale.

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1. Introduction

The main therapeutic intervention in rheumatoid arthritis (RA) is treatment with medications that suppress disease activity, articular disruption and inflammation [1,2]. However, the disadvantages of medications include side effects, cost, maintenance of effective long-term therapy and nullification of therapeutic effects.

Aside from disease-modifying medications, non-pharmacological approaches, such as nutritional therapy can reportedly suppress disease activity [3–6]. Such interventions include vegetarian, eliminate and elemental diets that primarily comprise vegetables that can reduce or eliminate food items that are thought to trigger RA symptoms. Although dietary therapy appears safe, dietary habits can be substantially altered, dropout rates are high and side effects include weight loss [5]. A Mediterranean diet that reflects the dietary habits and foods commonly consumed in Mediterranean countries is characterized by a high proportion of plant foods (fruits, vegetables, grains, pulses, nuts, seeds and olive oil), a low content of red meat and dairy products and modest alcohol intake. This diet can suppress disease activity in patients with RA [7,8]. This diet often requires a change in food consumption habits, but it is considered not to involve extreme dietary restrictions, as historically demonstrated by the population of the Mediterranean countries. Adopting a Mediterranean diet is considered less burdensome for patients than vegetarian, elimination and elemental diets [5].

Adopting this diet often requires changes in food and nutrient intake and which components suppress RA disease activity have not been defined.

One study has shown that the abundant monounsaturated fatty acids (MUFA) in olive oil affect RA disease activity [9]. However, some methodological aspects of that study are limited. Thus, the present study aimed to identify components of the Mediterranean diet that suppress RA disease activity in patients and provide the basis for an effective and minimally burdensome dietary intervention to achieve the same goal.

2. Materials and methods

2.1. Study population

We analyzed data from the prospective TOMORROW (The TOtal Management Of Risk factors in Rheumatoid arthritis patients to lOWer morbidity and mortality) cohort study of patients with and without RA that started during 2010 and will conclude in 2020. Details of the study participants and objectives have been published [10,11]. Table 1 shows a cross-sectional analysis of baseline data from 2011 in the prospective cohort study. The year 2010 included 208 consecutive patients with RA treated at the Department of Orthopaedic Surgery and Rheumatosurgery, Osaka City University Hospital (Osaka, Japan). A control group comprised 205 age- and sex-matched healthy volunteers who were recruited through mass media. Sequential differences in the effects of medications were compared within the RA group among whom 50% each were medicated with non-biological and biological agents. From 2010 to 2011, six and three participants in the RA and control groups, respectively, dropped out or experienced a fatal event (Fig. S1). All patients who fulfilled the 1987 revised American College of Rheumatology (ACR) classification criteria for RA [12] and the volunteers provided written informed consent in accordance with the Declaration of Helsinki. The Ethics Committee at Osaka City University Medical School approved the study protocol. This study is registered in the UMIN Clinical Trials Registry under UMIN000003876.

3. Methods

3.1. Participant assessment

All participants were assessed at our hospital. Height and body weight were measured simultaneously using an automatic stadiometer and weight scale (AD-6228AP, A&D Medical, Tokyo, Japan) in the morning after an overnight fast, and the BMI (body mass index) was calculated as the body mass (kg) divided by the square of the body height (m^2). All participants completed a self-administered questionnaire to determine their general health status.

3.2. Clinical assessment

Disease activity of RA was assessed using the disease activity score (DAS) in 28 joints (DAS28) and the erythrocyte sedimentation rate (ESR) [13], and functional status was assessed using the modified health assessment questionnaire (mHAQ) [14]. Tenderness and swelling were assessed in 28 joints (TJC and SJC, respectively). General health (GH) was globally assessed on a 100-mm visual analog scale (VAS). The patients with RA were sub-classified according to the European League Against Rheumatism (EULAR) criteria [15] using the calculated DAS28–ESR as being in remission or having low (LDA), moderate (MDA) or high (HDA) disease activity defined as DAS <2.6, 2.6 to <3.2, 3.2 to ≤5.1 and >5.1.

3.3. Daily nutrient intake status and Mediterranean diet score

Daily nutrient intake status was assessed in 2011 using the brief self-administered diet history questionnaire (BDHQ) [16,17], which was distributed to the study participants before starting the study and completed at home during the spring of 2011. The BDHQ measured the amount of food and nutrients consumed during the month before the investigation day. Dietitians checked for inappropriate or missing responses and ensured that the participants provided complete answers where necessary at the hospital. Based on a reported method [18], one participant from RA group and one from the control group who reported energy intake <600 kcal was omitted from the analysis. Nutrient and food intake is presented as g/1000 kcal.

Mediterranean diet scores were calculated using the food and nutrient intake status of the control group as a reference [19,20]. The ratio of monounsaturated fatty acids to saturated fatty acids (MUFA/SFA) and the intake of pulses, seafood, total grains (grains, tubers, and roots), fruits and vegetables was calculated as g/1000 kcal. The median was calculated using data from men and women in the control group. Intake above and below the median was scored as 1 point and 0, respectively. Conversely, intake of meat, milk and other dairy products above and below the median was scored as 0 and 1, respectively. Adequate alcohol intake for women (5–25 g) and men (10–50 g) was scored as 1 and values above or below these ranges were defined as inadequate and scored as 0. The Mediterranean diet scores ranged from 0 to 9, with higher scores indicating greater compliance with the diet. None of the patients in the present study scored 9.

3.4. Statistical analysis

Descriptive statistics are presented as numbers (%) or medians (25th–75th percentiles). All data were analyzed using SPSS II for Windows version 11.0.1J (SPSS Japan Inc., Tokyo, Japan). Gaussian distribution of the data was determined using the Shapiro–Wilk

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