THU0679

ADHERENCE TO THE MEDITERRANEAN DIET AND RISK OF RHEUMATOID ARTHRITIS IN THE FRENCH PROSPECTIVE E3N COHORT STUDY

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Background: The Mediterranean diet (MD), widespread in Southern European countries, mainly consists of olive oil, cereal products, fresh or dried fruit and vegetables, nuts, a moderate amount of dairy and meat, and many condiments and spices. It has been associated with significant reduction of overall mortality, cardiovascular diseases, and neoplastic diseases. It has been suggested to have a beneficial effect on rheumatoid arthritis (RA) activity due to its richness in antioxidants and unsaturated fatty acids. However, data on MD as a prevention of RA are limited.

Objectives: To assess the association between adherence to MD and risk of RA in a general population cohort.

Methods: The E3N cohort study (*Etude Epidémiologique auprès des femmes de la Mutuelle générale de l'Education Nationale*) is a French prospective cohort of 98,995 healthy women included in 1990-91 and followed since then (median follow-up of 28 years). Among women who completed a food-frequency questionnaire, we calculated the modified MD score (from 0 to 9) according to the consumption status of nine food components. Incident RA cases were detected using a validation process using a specific validation questionnaire and a drug reimbursement database. Hazard ratios (HRs) and 95% confidence intervals (CIs) for incident RA were estimated using Cox proportional hazards regression models with age as the time scale, and adjusting for known risk factors of RA and potential confounders. Because of the known importance of smoking on RA risk, we performed analyses adjusted and stratified on the smoking status.

Results: Among 62,630 women, 480 validated incident RA cases were diagnosed after a mean ($\pm$ standard deviation) of 11.7 ($\pm$ 5.9) years after the food-frequency questionnaire. In the whole population, high adherence to MD was not associated with a decreased risk of RA (HR for a 6-9 vs. 0-3 score = 0.86, 95% CI: 0.68–1.09, $P_{\text{linear trend}}$ = 0.11). However, among ever-smoking women (current or past smokers), high adherence to MD was associated with a decreased risk of RA (HR for a 6-9 vs. 0-3 score = 0.77, 95% CI: 0.53–1.05; $P_{\text{linear trend}}$ = 0.025), while there was no association in non-smokers (HR for a 6-9 vs. 0-3 score = 0.98, 95% CI: 0.70–1.38, $P_{\text{linear trend}}$ = 0.90).

HR (95% IC) for RA according to the MD score

MD score	[0-3]	[4-5]	[6-9]	P for trend
All population (N = 62,630)				
Cases no./person-years, no.	152/372,306	211/575,893	118/325,196	
Age adjusted	1	0.89 (0.72-1.10)	0.86 (0.68-1.09)	0.11
Multivariate*	1	0.89 (0.72-1.10)	0.86 (0.67-1.10)	0.1098
Ever smokers (N = 29,072)				
Cases no./person-years, no.	73/165,745	101/270,722	57/154,709	
Age adjusted	1	0.78 (0.58-1.04)	0.74 (0.53-1.05)	0.0247
Multivariate*	1	0.79 (0.58-1.06)	0.77 (0.54-1.09)	0.0444
Non smokers (N = 33,558)				
Cases no./person-years, no.	73/206,562	110/305,171	61/170,488	
Age adjusted	1	1.01 (0.75-1.36)	0.98 (0.70-1.38)	0.9011
Multivariate*	1	0.99 (0.74-1.34)	0.96 (0.68-1.35)	0.7725

* HRs were adjusted for age, educational level, body mass index, smoking status, passive smoking during childhood, energy intake, physical activity, gastrointestinal transit.

Conclusion: High adherence to a MD could reduce RA risk in ever-smoking women. Further studies are needed to confirm our findings.

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ANTI-PEPTIDYL-ARGININE DEIMINASE 3 AND 4 AUTOANTIBODIES IN A COHORT OF RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) affects up to 30% of patients with rheumatoid arthritis (RA). Peptidyl-arginine deiminases (PAD) are key enzymes in RA pathogenesis as they are involved in the citrullination of proteins, targets of anti-citrullinated protein antibodies (ACPA). Although RA-ILD significantly contributes to disease burden including mortality, diagnostic and prognostic biomarkers are still lacking.

Objectives: To measure anti-PAD3 and anti-PAD4 antibodies in a cohort of RA and compare their prevalence in patients with and without ILD. To assess the associations of anti-PAD3, anti-PAD4 and ACPA with disease activity, joint erosions, lung involvement and smoking history.

Methods: A total of 71 patients fulfilling the 2010 ACR/EULAR RA Classification Criteria were recruited; the mean age was 63.3 $\pm$ 12.4 and 87% of them were females, 11 (15.5%) of them had been diagnosed with ILD. Demographic, clinical as well as radiological data were retrospectively collected. ILD was defined as usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP) or indeterminate patterns on chest high-resolution computed tomography, according to ATS/ERS guidelines. Particle-based Multi-Analyte Technology (PMAT) (Inova Diagnostics, USA, research use only) was used to measure anti-PAD3 and anti-PAD4 autoantibodies. ACPA IgG were measured by chemiluminescence (QUANTA Flash CCP3, Inova Diagnostics, USA).

Results: Anti-PAD4 levels were correlated with erosive disease ($p=0.043$) and morning stiffness ($p=0.031$). Anti-PAD3 and anti-PAD4 levels were associated to DAS28-ESR at the time of sampling (anti-PAD3, $r=0.34$, $p=0.004$; anti-PAD4, $r=0.34$, $p=0.004$). Anti-PAD4 antibodies were significantly lower in patients with ILD ($p=0.043$). There was no association between anti-PAD4 and smoking, while anti-PAD3 antibodies were higher in non-smokers ($p=0.004$). A strong correlation was found between anti-PAD4 and anti-PAD3 levels ($r=0.73$, $p<0.0001$).

Conclusion: In our cohort, anti-PAD4 antibodies were correlated with joint erosions and RA disease activity, whereas a negative association with ILD was found. Smoking history was not associated with the presence and levels of anti-PAD antibodies. Our data validate the usefulness of anti-PAD4 antibodies as a biomarker for erosive disease. Further studies that take into account relevant confounders like therapy and larger RA-ILD cohorts are needed.

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SEXUAL FUNCTION AND REPRODUCTION CAN BE IMPAIRED IN MEN WITH RHEUMATIC DISEASES: A SYSTEMATIC REVIEW

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Background: Sexual function and reproduction are important aspects of quality of life for the majority of men (1,2). In the last decade inflammation has been associated with male factor infertility and sexual dysfunction (3,4). Because many patients with rheumatic diseases have a

chronic state of inflammation, it is reasonable to believe that this can result in impaired sexual function and reproduction. Previous research on this topic in Rheumatology mainly focused on the effect of drugs on fertility parameters.

Objectives: Our objective is to summarize the information on the influence of rheumatic diseases on male sexual function and reproduction.

Methods: A systematic search of Embase, Medline, Web of science and Cochrane Central was carried out in May 2018 to find relevant papers. The search strategy was extensive and included a complete list of immune mediated diseases from Rheumatology, Dermatology and Gastroenterology and several keywords for our outcomes (sexual function, fertility and pregnancy outcome). This review was registered in PROSPERO (5). The search yielded 6568 articles. Titles and abstracts were screened independently by LP and JC, resulting in 177 papers selected for full text review. Methodological quality of the studies was assessed with the Newcastle Ottawa Scale (6).

Results: Regarding rheumatic diseases a total of 104 papers were included in the final analysis. 4 diseases (Spondyloarthropathies (SpA), Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE) and Systemic Sclerosis (SSc)) represented 60% of the articles. The overall quality of the studies was low to moderate.

Sexual dysfunction (SD) is a common problem for patients with rheumatic diseases and it is usually undiagnosed. It was reported in approximately half of men with RA, SLE and SpA and in almost all the men diagnosed with SSc. It should be noted that, although in several studies increasing age was correlated with a higher prevalence and severity of SD, young patients with SpA or SLE can also be affected.

Regarding fertility and reproduction, different results per disease were found. Hypogonadism might be a common problem in men with RA and SLE. Many men with SLE and RA have endocrine axis abnormalities. Interestingly, these disturbances were not detected in SpA patients (See Table 1). Semen quality abnormalities are frequent in SLE patients and this was found to be associated not only with medication toxicities but also with disease activity. The number of children of male patients diagnosed with SLE and SSc was lower than healthy controls.

A brief summary of our findings per disease are presented in Figure 1.

Conclusion: Our findings suggest that not only medication can have detrimental effects on sexual function and reproduction of men with rheumatic diseases but also the disease itself. Therefore, clinicians should be aware of a high prevalence of sexual and reproduction problems in this population and take this into account when counseling them. More research focusing on this association is needed.

Disease	Outcome	
RA	Sexual dysfunction	Prevalence: 33-62% [range] in 282 patients compared to 11-40% [range] 140 controls. Main correlations: Age, pain, fatigue. Almost 30% of patients want advice on this topic.
	Hormones	Lower serum testosterone levels. Lower LH levels. Testosterone levels increased in a group of patients that responded to treatment.
	Pregnancy outcomes	Paternal RA was not associated with preterm birth or fetal growth abnormalities compared to the general population. No higher risk of serious congenital malformations.
SLE	Sexual dysfunction	Prevalence: 12-69% [range] in 245 patients compared to 0-22% [range] 197 controls. Main correlations: Arterial events, SLICC damage score, persistent lymphopenia, lower median penis circumference. In one study: 81% of patients considered it would be appropriate to be asked about their sexual function Median of FSH and LH were significantly higher in SLE patients versus controls.
	Hormones	
	External genitalia	Reduction of testicular volume correlates with semen quality abnormalities.
	Semen quality	Sperm concentration and motility was abnormal in a significant proportion of patients. High FSH levels correlated with sperm abnormalities.
SpA	Pregnancy outcomes	Percentage of partner with gestation was statistically lower in SLE patients compared to controls: • 20% vs 60%
	Sexual dysfunction	Prevalence: 32-63.6% [range] in 856 patients compared to 14.6-51.9% [range] in 580 controls. Main correlations: Disease activity and duration, depression, fatigue. In one study: 95.9% had never been asked by any doctors about sexual activity.
	Hormones	No differences in FSH, LH and testosterone among patients and controls.
	External	No differences in testicular volume among patients and

Figure 1:

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THU0682 UNDERDIAGNOSIS OF TRADITIONAL CARDIOVASCULAR RISK FACTORS IN RHEUMATIC DISEASES

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Background: Patients with rheumatic diseases (RD) have a higher cardiovascular risk (CVR), compared to the general population (1). The increased risk, in this population, tends to be associated with the chronic inflammation generated by RD. Another contributor is the coexistence of traditional CVR factors, such as diabetes, hypertension, obesity, smoking, and dyslipidemia (2). It is known that adequate control of this factors can reduce the overall CVR. Due to the increased CVR burden, there's a growing awareness of cardiovascular assessment in rheumatic patients. Therefore, the 2016 EULAR guidelines recommend making this assessment every 5 years, in order to decrease their morbidity and mortality by early treatment.

Figure 1. Traditional cardiovascular risk factors.

Objectives: To determine the prevalence of underdiagnosis and inefficient treatment of traditional cardiovascular risk factors in RD patients.

Methods: A cross-sectional, observational study of patients between 30 and 75 years with rheumatoid arthritis (RA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE) and ankylosing spondylitis (AS) recruited at the rheumatology clinic at a University Hospital in northeastern Mexico. Exclusion criteria: previous cardiovascular disease, overlap syndromes, diabetes, or pregnancy. Evaluation included history of lifestyle, comorbidities, medications, blood pressure, anthropometry and fasting glucose measures. Framingham-BMI (FRS-BMI) was used to calculate their predicted CVR to 10 years.

Results: A total of 382 patients were recruited, 90.6% were women (n=346), with a median age of 53 years (45-59). In this population, 87.4% of the patients (n=334) had at least one CVR factor; the presence of traditional CVR factors according to RD is shown in Figure 1. Other population characteristics are in Table 1. Around half of the patients were not in their ideal weight, 32% being diagnosed as overweight and 31.4% with obesity. Out of the patients with no previous diagnosis of hypertension (n=350, 91.5%), 36.1% had elevated or high blood pressure levels. The patients that did have previous diagnosis, 68.7% didn't have an adequate control of their blood pressure, even though they're on pharmacological treatment. History of dyslipidemia was found in 5.2% of patients. Half of them arrived at consultation with a recent lipid profile, having a median LDL of 133.5 (109-158) mg/dL, not meeting target levels. Even though no diabetic patients were included, 20.8% of the patients had hyperglycemia. According to FRS-BMI, 80.4% of the patients had a low CVR, 14.9% moderate risk, and 4.7% had a high CVR.