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### 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)	<b>0,0247</b>
Multivariate*	1	0.79 (0.58-1.06)	0.77 (0.54-1.09)	<b>0,0444</b>
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.

#### REFERENCES:

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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