Table 1. The levels of Leptin and Adiponectin in RA patients and controls at BL and 5Y, and the changes of them from BL to 5Y

		RA	Controls	p
BL	Leptin (ng/ml)	7.43	5.63	0.006
	Adiponectin (µg/ml)	16.67	14.41	0.007
5Y	Leptin (ng/ml)	10.89	8.18	0.004
	Adiponectin (µg/ml)	19.79	13.76	<0.001
Δ5Y-BL	Leptin (ng/ml)	3.46	2.55	0.232
	Adiponectin (µg/ml)	3.12	-0.64	<0.001

Table 2. The levels of Leptin and Adiponectin at BL and 5Y in RA patients with and without biologic treatment at BL.

		Biologics (+)	Biologics (-)	p
BL	Leptin (ng/ml)	6.85	8.09	0.126
	Adiponectin (µg/ml)	17.97	15.20	0.020
5Y	Leptin (ng/ml)	10.18	11.69	0.157
	Adiponectin (µg/ml)	22.17	17.16	0.005
Δ5Y-BL	Leptin (ng/ml)	3.34	3.59	0.419
	Adiponectin (µg/ml)	4.15	1.96	0.032

Speakers bureau: Daiichi Sankyo Co. Ltd., Mitsubishi Tanabe Pharma, Janssen Pharmaceutical K.K., Astellas Pharma Inc., Takeda Pharmaceutical Co. Ltd., Ono Pharmaceutical Co. Ltd., Abbvie GK, Pfizer Inc., Eisai Co., Ltd., Chugai Pharmaceutical Co., Ltd., Tadashi Okano Grant/research support from: AbbVie, Eisai, Mitsubishi Tanabe Pharma Corporation and Nipponkayaku, Speakers bureau: AbbVie, Asahikasei, Astellas Pharma Inc, Ayumi Pharmaceutical, Bristol-Myers Squibb, Chugai Pharmaceutical, Daiichi Sankyo, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, Novartis Pharma, Ono Pharmaceutical, Pfizer, Sanofi, Takeda Pharmaceutical, Teijin Pharma and UCB, Yuko Sugioka: None declared, Masahiro Tada: None declared, Tatsuya Koike Grant/research support from: AbbVie, Astellas Pharma Inc, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Speakers bureau: AbbVie, Astellas Pharma Inc, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen, Lilly, Mitsubishi Tanabe Pharma Corporation, MSD, Ono Pharmaceutical, Pfizer, Roche, Takeda Pharmaceutical, Teijin Pharma, and UCB, Hiroaki Nakamura Grant/research support from: Astellas Pharma Inc. and Asahi Kasei Pharma Co.

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SAT0045

DISTRIBUTION AND SEVERITY OF PERIODONTITIS PREDICTS PROGRESSION TO INFLAMMATORY ARTHRITIS IN ANTI-CCP POSITIVE AT-RISK INDIVIDUALS WITHOUT CLINICAL SYNOVITIS

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Background: The prevalence of periodontal disease and the citrullinating bacterium *Porphyromonas gingivalis* are increased in anti-CCP positive individuals at-risk of rheumatoid arthritis (RA) (1). This suggests periodontal inflammation may have an important role in the initiation and development of RA. Despite significant interest in the role of the periodontium and other mucosal sites in the initiation of RA-related autoimmunity, the influence of mucosal inflammation on progression to inflammatory arthritis (IA) in at-risk individuals remains unclear.

Objectives: To investigate the association between periodontitis and progression to inflammatory arthritis in anti-CCP+ at-risk individuals without synovitis.

Methods: Anti-CCP positive individuals with musculoskeletal symptoms but no clinical synovitis (CCP+ at-risk) were recruited as part of a national prospective cohort study. Comprehensive periodontal examination was performed at baseline by a dentist; six sites per tooth were assessed for clinical attachment level (CAL), pocket depth (PD) and bleeding on probing (BOP). Periodontal disease sites (PDD) were defined as CAL ≥2mm and PD ≥4mm. The distribution of PDD was classified in line with recent guidelines (2). The severity i.e. total burden of periodontal inflammation, was quantified at patient level using the periodontal inflamed surface area (PISA) index(3). CCP+ at-risk were monitored for progression to IA. Multivariable Cox regression was used to assess the effect of PDD distribution and PISA on progression to IA.

Results: 126 CCP+ at-risk underwent full periodontal examination and were followed up for median 23.4 months (range 0.6 – 56.8 months). Mean age was 49 years, 86 (68%) were females. At baseline, 42(33%) subjects had no PDD, 51(40%) had localised PDD (<30% teeth with one or more PDD site) and 33 (26%) had generalised PDD (≥ 30% of teeth with one or more PDD site). Mean (SD) PISA for all subjects was 267(319)mm². 31 subjects (25%) progressed to IA after median of 12.6 months (range 0.6 – 49.5 months). Progression to IA was significantly higher in subjects with localised PDD compared with those without PDD (33% vs 16%, HR (95% CI) 2.45 (1.02, 5.94) p=0.02), figure 1. Interestingly, this association was not seen in subjects with generalised PDD (19% progression, HR 0.68 (0.20, 2.32). In addition, severity (i.e. total burden) of periodontal inflammation (PISA) was not significantly predictive of progression to IA alone (HR 1.001 (0.999-1.002), p=0.08). However, when adjusting for distribution of PDD, PISA was significantly associated with progression to IA (HR 1.0016 (1.0003- 1.003), p=0.00163).

Conclusion: Periodontal inflammation predicts progression to IA in CCP+ at-risk individuals without clinical synovitis. The severity (i.e. total burden) of periodontitis appears to be particularly predictive of progression to IA in patients with localised periodontitis. These data suggest periodontitis may be an important factor in the development of RA and provide rationale for periodontal intervention with the aim of arthritis prevention in at-risk individuals.

References:

- [1] Mankia K et al, JAMA Network Open(2019)
- [2] Caton J et al, J Clin Periodontol(2018)
- [3] Nesse W et al, J Clin Periodontol(2008)

Figure 1: Survival plot of anti-CCP positive at-risk individuals showing cumulative inflammatory arthritis-free survival according to the distribution of periodontal disease sites at baseline. Localized PDD; periodontal disease sites in <30% of teeth. Generalized PDD; periodontal disease sites in ≥30% of teeth.

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