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## OP0076 RISK OF DEVELOPING ADDITIONAL IMMUNE MEDIATED MANIFESTATIONS FOR PATIENTS WITH SYSTEMIC ARTHRITIDES

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**Background:** Patients with the systemic arthritides ankylosing spondylitis [AS], psoriatic arthritis [PsA], rheumatoid arthritis [RA] may develop additional, non-musculoskeletal immune mediated manifestations (nms-IMMs).
**Objectives:** To compare the risk of developing nms-IMMs between patients with and without an existing AS, PsA, or RA.
**Methods:** Risk for nms-IMMs was estimated in the MarketScan Commercial Claims and Encounters database (1/2006–9/2015) for case patients with AS, PsA, RA (the "systemic arthritides"). Up to 1,000 controls were matched with replacement by age, sex, state of residence and insurance type to case patients aged 18–64. The systemic arthritides ("cases") were identified by ICD-9 diagnosis codes on ≥2 medical claims ≥30 days apart. A case patient's earliest nms-IMM claim was designated as the index date for the case and all matched controls. Onset of 6 nms-IMDs was identified by the first post-index claim: celiac disease [CE], hidradenitis suppurativa [HS], inflammatory bowel disease [IBD], lupus [SLE], psoriasis [PsO], uveitis [UV]; some of these are well-known manifestations of seronegative spondylarthropathies, like PsA and AS; some are not. All subjects had continuous health plan enrollment for ≥365 days before and after index date. Cumulative incidence of nms-IMMs was assessed at 5 years. Their risk was analyzed with stratified Cox proportional hazards models. Standard errors were adjusted for clustering by case-control match group.
**Results:** Among 117,794 cases, mean age was 49 years and 71% were female. Mean number of matched controls per case was 664. Across the 3 initial cohorts of patients with AS, PsA, or RA, median follow-up ranged 939–972 days for cases and 931–950 days for controls. Among case patients, 5-year cumulative incidence of any nms-IMM occurrence was 17.5% for AS, 41.8% for PsA, and 14.4% for RA. Patients with nms-IMMs had significantly higher risk than matched controls of developing each, any 1, or any 2 of the 6 manifestations (P≤0.002) (Table).

| Initial IMID | | Secondary IMID | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | CE | HS | SLE | PsO | UV | IBD | 1st of Any 1 | 2nd of Any 2 |
| AS | N Cases | 6,339 | 6,344 | 6,282 | 6,275 | 6,103 | 6,263 | 6,352 | 6,352 |
| | 5-yr Incidence | 0.9 | 0.2 | 2.9 | 4.2 | 7.7 | 3.4 | 17.5 | 1.2 |
| | Hazard Ratio | 11.2 | 3.3 | 23.7 | 8.6 | 54.9 | 16.0 | 17.9 | 24.6 |
| PsA | N Cases | 8,382 | 8,389 | 8,311 | 6,111 | 8,351 | 8,347 | 8,406 | 8,406 |
| | 5-yr Incidence | 0.5 | 0.6 | 2.1 | 51.0 | 1.8 | 1.7 | 41.8 | 2.5 |
| | Hazard Ratio | 5.3 | 10.5 | 14.1 | 163.2 | 10.0 | 7.3 | 50.9 | 43.3 |
| RA | N Cases | 102,708 | 102,810 | 100,414 | 101,965 | 102,424 | 102,318 | 103,036 | 103,036 |
| | 5-yr Incidence | 1.0 | 0.5 | 7.5 | 3.4 | 1.5 | 1.8 | 14.4 | 1.0 |
| | Hazard Ratio | 10.3 | 8.1 | 55.3 | 7.2 | 8.2 | 7.6 | 14.1 | 14.3 |

Notes: Hazard ratios from Cox proportional hazards models. Hazard ratios >1 indicate higher risk for case patients relative to controls. All hazard ratios are significant at P<0.002.

**Conclusions:** The risk of developing non-musculoskeletal manifestations was significantly higher for patients with AS, PsA, and RA than for matched controls. These included not only the well-known manifestations of PsA and AS but also others like manifestations leading to claims for SLE, celiac disease or HS. When managing these systemic arthritides, surveillance for additional immune mediated manifestation is warranted.
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## OP0077 PRIMARY PROPHYLAXIS FOR PNEUMOCYSTIS PNEUMONIA IN PATIENTS WITH RHEUMATIC DISEASE AND TREATED WITH PROLONGED, HIGH-DOSE STEROID: A RETROSPECTIVE COHORT STUDY WITH 12-YEAR OBSERVATION

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**Background:** Pneumocystis pneumonia (PCP) is a significant cause of morbidity and mortality in patients with rheumatic diseases, especially in the case of patients receiving high-dose steroid treatment.
**Objectives:** To investigate the efficacy and safety of PCP prophylaxis using trimethoprim/sulfamethoxazole (TMP-SMX) in patients with rheumatic disease receiving prolonged, high-dose steroids
**Methods:** This study includes 1522 cases of prolonged (≥4 weeks), high-dose (≥30mg/day prednisone or equivalent) steroid treatment from 1092 patients with any rheumatic diseases during a 12-year period in a single tertiary referral center in South Korea. Of them, prophylactic TMP-SMX was administered in 262 cases (prophylaxis group) with a mean (SD) duration of 229.0 (272.7) days whereas other 1260 cases received no prophylaxis (control group). Primary outcome was 1-year incidence of PCP between the two groups. Secondary outcomes included PCP-related mortality, ICU admission rate, all-cause in-hospital mortality and incidence of any adverse drug reactions (ADRs) of TMP-SMX. To minimize the baseline imbalance between the two groups, we introduced propensity-score matching and performed the same analysis in the post-matched population as a sensitivity analysis.
**Results:** Patients in the prophylaxis group were treated more often with secondary immunosuppressive drugs and had a higher proportion of patients with PCP high-risk diseases (ANCA-associated vasculitis and dermatomyositis) and lymphopenia at baseline. Overall, 30 cases of PCP occurred and resulted in death in 11 cases (36.7%). In the prophylaxis group, only one non-fatal case of PCP occurred. One-year PCP incidence was significantly lower in the prophylaxis group (adjusted HRs=0.096 [0.013–0.719]) (Figure). TMP-SMX also significantly reduced the PCP-related mortality (adjusted HR=0.101 [0.001–0.809]) whereas

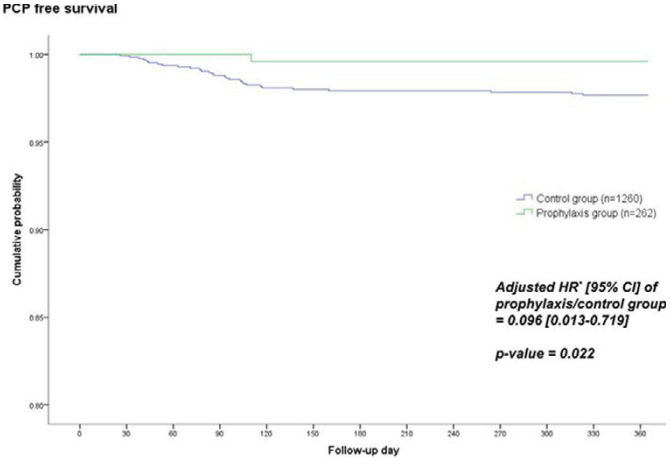


**Figure. Kaplan-Meier curve of 1-year incidence of PCP between the two groups**

*, HR was adjusted for patient's age, concomitant cyclophosphamide pulse and baseline lymphopenia

ICU admission rate and in-hospital mortality rate were not different between the two groups during the observation. This result was consistent in the sensitivity analysis where same analysis was performed in the post-matched population.
Thirty-four cases of ADRs of TMP-SMX occurred, with an incidence rate (95% CI) of 24.2 (17.3–33.0) per 100 person-year. There were two cases of serious ADR (one pancytopenia and one Steven's Johnson syndrome) but they all recovered shortly after the discontinuation of TMP-SMX. The number needed to harm (NNH) of serious ADR was 109 whereas the number needed to treat (NNT) to prevent one case of PCP in the whole population was 52.
**Conclusions:** In patients with rheumatic disease receiving prolonged, high-dose steroid treatment, TMP-SMX prophylaxis significantly lower the incidence of PCP with favorable safety.
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## OP0078 THE LONG TERM PROGNOSTIC SIGNIFICANCE OF PULMONARY HYPERTENSION IN SARCOIDOSIS - A BIG DATA ANALYSIS

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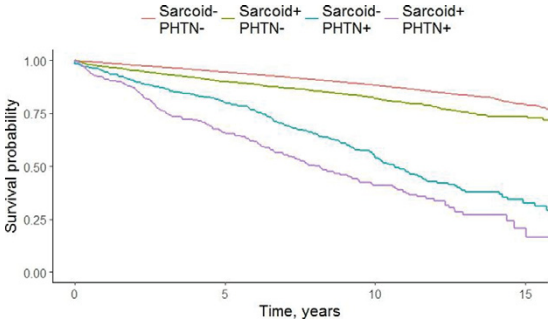
**Background:** Sarcoidosis is a multisystem, chronic, progressive, granulomatous disease. Sarcoidosis-associated pulmonary hypertension is well described, but not common complication of sarcoidosis[1]. In small scale studies, it has been previously described as a manifestation of advanced disease and was found to be associated with increased morbidity and mortality[2]. Previous studies have shown that treatment may be safe and improve pulmonary hemodynamics in sarcoidosis-associated pulmonary hypertension[3,4]. However, big data analyses regarding the exact magnitude and prognosis of sarcoidosis-associated pulmonary hypertension are lacking.
**Objectives:** To assess the long-term prognostic significance of sarcoidosis-associated pulmonary hypertension using a big data registry with a 15-year follow-up period.
**Methods:** Utilizing the medical records of Clalit Health Services, the largest HMO in Israel, we extracted a cohort consisted of sarcoidosis patients along with their age-and-sex matched controls. Dates of registration in the medical records of sarcoidosis, pulmonary hypertension and death, as well as anthropometric information and medical comorbidities were extracted from the database. To compare the distribution of variables across the cohort strata, univariate analysis was performed using Chi-square and student t-test. Multivariate analysis using a logistic regression model was used to find variables associated with pulmonary hypertension. Survival analysis using cox proportional hazards method and log-rank test was performed to find variables associated with increased risk of all-cause mortality.
**Results:** The cohort included 3,993 sarcoidosis patients and 19,856 age-and-sex matched controls. The mean age of both groups was 56, and both consisted about 63% females. Pulmonary hypertension was observed among 269 sarcoidosis patients (6.74%) vs. 400 controls (2.01%), $p<0.001$. In multivariate analysis, sarcoidosis was found to be independently associated with diagnosis of pulmonary hypertension (OR 3.09, 95% CI 2.6–3.67). After more than 15 years of follow-up, 710 (17.8%) of the sarcoidosis patients had died, compared to 2121 (10.7%) of the controls ($p<0.001$). In multivariate survival analysis, both sarcoidosis and pulmonary hypertension were found to be significantly associated with increased risk to all-cause mortality (HR 1.83, 95% CI 1.66–2.02 and HR 2.32, 95% CI 2.05–2.63, respectively).




**Conclusions:** Sarcoidosis-associated pulmonary hypertension is associated with poor prognosis. Proper screening methods are recommended to assess whether early identification and treatment may improve life expectancy.

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## OP0079 BODY FAT PERCENTAGE AND WAIST CIRCUMFERENCE WERE ASSOCIATED WITH THE DEVELOPMENT OF RHEUMATOID ARTHRITIS – A DANISH FOLLOW-UP STUDY

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**Background:** Several studies have investigated the association between overweight and the development of rheumatoid arthritis (RA) and have come out with conflicting results. Body Mass Index (BMI) has been the preferred surrogate measure for overweight in these studies. However, BMI correlates only modestly with total amount of body fat and does not reflect fat distribution.
**Objectives:** To investigate the association between BMI, waist circumference, bio-impedance-derived total body fat percentage and the incidence of RA.
**Methods:** A population-based cohort study conducted within the Danish Diet, Cancer and Health cohort, which included individuals aged 50 to 64 years at the recruitment in the period between 1993 and 1997. Body fat composition measurements and data on lifestyle factors were collected at the enrolment into the cohort. The participants who subsequently developed RA were identified via linkage to The Danish National Patient Registry. The participants were followed until development of RA, death, loss to follow-up or October 2016, whichever came first. Data were analyzed by Cox proportional hazards regression model with delayed entry and age as the underlying time variable. Analyses were stratified by gender. Cox regression analyses with restricted cubic spline were carried out to elucidate the dose-response association between anthropometric measures and risk of RA. Smoking, socio-economic status, alcohol consumption, physical activity and intake of n-3 fatty acids were included in multivariate analyses as potential confounders.

Table 1. Cox proportional hazard ratios for association between body composition measurements and incidence of RA

| Variable | Hazard ratio (95% confidence interval)) Multivariable adjusted* | |
|---|---|---|
| | Men | Women |
| BMI <18.5 kg/m$^2$ | N/A | 0.86 (0.21 -3.48) |
| BMI 18.5–24.99 kg/m$^2$ | 1 (ref) | 1 (ref) |
| BMI 25–29.99 kg/m$^2$ | 0.83 (0.55–1.24) | 1.48 (1.14 – 1.91) |
| BMI >30 kg/m$^2$ | 0.69 (0.37–1.30) | 1.54 (1.09 – 2.17) |
| Abdominal obesity (waist circumference >102 cm for men, >88 cm for women) | | |
| No | 1 (ref) | 1 (ref) |
| Yes | 1.16 (0.75–1.80) | 1.24 (0.96–1.61) |
| | Hazard ratio (95% confidence interval) per 1% increment of body fat Multivariable adjusted* | |
| | Men | Women |
| Fat percentage | 0.99 (0.96–1.03) | 1.03 (1.01–1.05) |

*Adjusted for age, smoking status, total tobacco consumption (g/day), smoking duration, alcohol consumption (g/day), socio-economic status, physical activity (Metabolic Equivalent of Task, MET), total intake of n-3 fatty acids.