FRIDAY, 05 JUNE 2020

Epidemiology, risk factors for disease or disease progression

FRI0531

AIR POLLUTANTS AND DEVELOPMENT OF INTERSTITIAL LUNG DISEASE IN PATIENTS WITH AUTOIMMUNE DISEASES

H. H. Chen^{1,2}, W. C. Chao³, Y. H. Chen², D. Y. Chen⁴, C. H. Lin¹. ¹Taichung Veterans General Hospital, Department of Medical Research, Taichung, Taiwan, Republic of China; ²Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Taichung, Taiwan, Republic of China; ³Taichung Veterans General Hospital, Department of Critical Care Medicine, Taichung, Taiwan, Republic of China; ⁴China Medical University Hospital, Rheumatology and Immunology Center, Taichung, Taiwan, Republic of China

Background: Interstitial lung disease (ILD) is characterized by progressive inflammation and fibrosis, and accumulating evidence have shown that exposure to air pollutants was associated with the development of ILD. Autoimmune diseases are highly correlated with ILD, including connective tissue disease-associated ILD (CTD-ILD) as well as interstitial pneumonia with autoimmune features (IPAF), and the development of ILD is a crucial cause of morbidity and mortality in patients with autoimmune diseases. One recent Taiwanese study reported that exposure to air pollutants was associated with incident systemic lupus erythematosus (SLE). However, the impact of air pollutants on the development of ILD among patients with autoimmune diseases remains unknown.

Objectives: The study aimed to address the impact of accumulating exposure to air pollutant above moderate level, defined by Air Quality Index (AQI) value higher than 50, on the development of ILD in patients with autoimmune diseases including SLE, rheumatoid arthritis (RA) and primary Sjögren's syndrome (SS).

Methods: We used a National Health Insurance Research Database in Taiwan to enroll patients with SLE (International Classification of Diseases (ICD)-9 code 710.0, n=13,211), RA (ICD-9 code 714.0 and 714.30–714.33, n=32,373), and primary SS (ICD-9 code, 710.0, n=15,246) between 2001 and 2013. We identified newly diagnosed ILD cases (ICD-code 515) between 2012 and 2013 and selected age, sex, disease duration and index-year matched (1:4) patients as non-ILD controls. The hourly levels of air pollutants one year prior to the index-date were obtained from 60 air quality monitoring stations across Taiwan, and the air pollutants in the present study consisted of particulate matter <2.5 µm in size (PM_{2.5}), particulate matter <10 µm in size (PM₁₀), nitrogen dioxide (NO₂), carbon monoxide (CO), sulfur dioxide (SO₂) and ozone (O₃). We used a spatio-temporal model built by a deep-learning mechanism to estimate levels of air pollutants at 374 residential locations based on data of 3 air quality monitoring stations near the location (8). Notably, we used cumulative exposed hours to air pollutants higher than modest level, defined by AQI criteria, given that daily mean level of air pollutants might possibly underestimate the triggered inflammatory effect by a temporary exposure of high-level air pollutant. A conditional logistic regression was used to determine the association between exposure to air pollutant and the development of ILD, adjusting age, gender, Charlson Comorbidity Index (CCI), urbanization, family income, and medications for autoimmune diseases.

Results: A total of 272 patients with newly diagnosed ILD were identified among patients with autoimmune diseases, including 39 with SLE, 135 with RA, and 98 with primary SS. We found that the duration of exposure to PM_{2.5} higher than modest level was associated with the risk of ILD development in patients with SS (adjOR 1.07, 95% CI 1.01–1.13), and similar trends

were also found in patients with SLE (adjOR 1.03, 95% CI 0.95–1.12) and RA (adjOR 1.03, 95% CI 0.99–1.07). Intriguingly, we observed an inverse correlation between the duration of exposure to O₃ and the development of ILD in patients with SS (adjOR 0.83, 95% CI 0.70–0.99); however, the finding was not found in patients with SLE (adjOR 1.13, 95% CI 0.92–1.37) and RA (adjOR 0.98, 95% CI 0.87–1.11).

Conclusion: In conclusion, we identified that longer exposure to PM_{2.5} higher than modest level tended to be associated with the development of ILD in patients with autoimmune diseases, mainly SS.

References:

- [1] Araki T, Putman RK, Hatabu H, Gao W, Dupuis J, Latourelle JC, et al. Development and Progression of Interstitial Lung Abnormalities in the Framingham Heart Study. *Am J Respir Crit Care Med* 2016;194:1514-1522.
- [2] Tang KT, Tsuang BJ, Ku KC, Chen YH, Lin CH, Chen DY. Relationship between exposure to air pollutants and development of systemic autoimmune rheumatic diseases: a nationwide population-based case-control study. *Ann Rheum Dis* 2019;78:1288-1291.

Disclosure of Interests: Hsin-Hua Chen: None declared, Wen-Cheng Chao: None declared, Yi-Hsing Chen Grant/research support from: Taiwan Ministry of Science and Technology, Taiwan Department of Health, Taichung Veterans General Hospital, National Yang-Ming University, GSK, Pfizer, BMS., Consultant of: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Lilly, GSK, AstraZeneca, Sanofi, MSD, Guigai, Astellas, Inova Diagnostics, UCB, Agnitio Science Technology, United Biopharma, Thermo Fisher, Gilead., Paid instructor for: Pfizer, Novartis, Johnson & Johnson, Roche, Lilly, AstraZeneca, Sanofi, Astellas, Agnitio Science Technology, United Biopharma., Speakers bureau: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Lilly, GSK, AstraZeneca, Sanofi, MSD, Guigai, Astellas, Inova Diagnostics, UCB, Agnitio Science Technology, United Biopharma, Thermo Fisher, Gilead., Der-Yuan Chen: None declared, Ching-Heng Lin: None declared

DOI: 10.1136/annrheumdis-2020-eular.204

FRI0532

THE IMPACT OF GENETICALLY DETERMINED SERUM URATE LEVELS ON THE DEVELOPMENT OF CARDIOVASCULAR DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS OF MENDELIAN RANDOMIZATION STUDIES

J. Choi¹, N. McCormick^{1,2}, S. Marozoff², M. De Vera², H. Choi^{1,2}. ¹MGH, Boston, United States of America; ²Arthritis Research Canada, Richmond, Canada

Background: Conventional observational studies have identified serum urate (SU) as an independent risk factor for cardiovascular diseases (CVDs),^{1,2} but the causal relationships remain unsettled, with potential confounding and reverse causality. When applied correctly, Mendelian randomization (MR) employing genetic variants as instrumental variables can eliminate these biases and allow for causal inference.

Objectives: To conduct a systematic review and meta-analysis of English-language, peer-reviewed MR studies on the causal effects of SU on CVDs and assess validation of key MR assumptions.

Methods: A research librarian conducted a search (inception to January 2020) of four databases (Medline, Embase, Cochrane Library, and Web of Science),

Fig. 1 : PRISMA flow diagram.

which was supplemented by hand-search. Titles and abstracts were screened by two independent reviewers, who subsequently evaluated and extracted data from full-text of selected articles. Pooled meta-analysis was performed using random-effects weighting.

Results: Of 1014 articles identified, 40 were selected for full-text review and 13 studies reporting on CVDs were included in the systematic review (Figure 1). The first was published in 2009 and five were published in 2018 or 2019 alone. The included studies were of varying quality in regards to satisfying the assumptions for MR design.

Overall, there was little evidence for a causal association between SU and risk of CVDs (Table 1). Random-effects meta-analysis revealed that SU was not significantly associated with risk of CVDs (OR=1.04; 95% CI=0.99-1.09) (Figure 2). 11 of the 13 studies reported null estimates for the effects of genetically-determined SU levels on CVDs. Two studies with small numbers of cases (N=125 and 222) reported significant associations, but these pertained to highly-specific subgroups.

Table 1. Summary of included studies. CAD: Coronary Artery Disease; CHD: Coronary Heart Disease; IHD: Ischaemic heart disease; MI: Myocardial Infarction; MR: Mendelian Randomization; PVD: Peripheral Vascular Disease; SNP: Single Nucleotide Polymorphism

First author; year	Number of SNPs analyzed	Outcome (n cases)	Power	MR criteria validated: 1. relevance 2. pleiotropy 3. confounding	Conclusion
Stark; 2009	10 separately	CAD (1,473)	30%-66%	1, 3	Null
Yang; 2010	8 combined	CHD (3,050)	<80%	1, 2, 3	Null
Palmer; 2013	1 (rs7442295)	IHD (3,742)	N/A	1, 2*, 3	Null
Kleber; 2015	8 combined	CAD (2,418)	N/A	1, 2, 3	Null
		PVD (295)			
Han; 2015	2 separately	CHD (1,146)	80%	1, 2*, 3	Null
Testa; 2015	1 (rs734553)	CVD events (CVD death, stroke, MI) (222)	N/A	1, 2*	Significant for CV events
White; 2016	31 combined	CAD (65,877)	83%	1, 2, 3	Null
Keenan; 2016	14 combined	CHD (54,501)	>80%	1, 2, 3	Null
		Stroke (14,779)			
Li; 2018	31 combined	IHD (9,467)	70%	1, 2, 3	Null
		MI (3,625)			
Li; 2019	31 combined	CHD (60,801)	N/A	1, 2, 3	Null
		MI (43,676)			
		Stroke (10,307)			
Macias-Kaufer; 2019	2 separately	CAD (704)	N/A	1, 2*, 3	Null
Efstathiadou; 2019	28 separately	CHD (184,305)	>80%	1, 2, 3	Null
		MI (54,162)			
		Stroke (514,791)			
Chiang; 2019	8 combined	CHD (125)	N/A	1, 2, 3	Significant for CHD
		Stroke (57)			

* Risk of pleiotropy (assumption 2) is low when utilizing few well-established SNPs

Fig. 2 : Pooled meta-analysis results.

Conclusion: Evidence from this systematic review does not support a causal role for SU levels and CVDs. As such, interventions targeting SU levels alone are unlikely to lower the risk of CVDs.

References:

- [1] Zhu Y, Pandya BJ, Choi HK. Comorbidities of gout and hyperuricemia in the US general population: NHANES 2007-2008. *Am J Med* 2012;125:679-87 e1.
- [2] Choi HK, Curhan G. Independent impact of gout on mortality and risk for coronary heart disease. *Circulation* 2007;116:894-900

Disclosure of Interests: Jeewoong Choi: None declared, Natalie McCormick: None declared, Shelby Marozoff: None declared, Mary De Vera: None declared, Hyon Choi Grant/research support from: Ironwood, Horizon, Consultant of: Takeda, Selecta, Horizon, Kowa, Vaxart, Ironwood

DOI: 10.1136/annrheumdis-2020-eular.6191

FRI0533

SMOKING AS A PREDICTIVE FACTOR FOR SPONDYLOARTHRITIS RELATED UVEITIS: RESULTS FROM A SINGLE CENTRE CROSS-SECTIONAL STUDY.

E. Costa¹, D. Almeida^{2,3}, M. Cerqueira², J. Redondo Costa², A. R. Ribeiro², J. Neves². ¹Hospital de Braga, Rheumatology, Braga, Portugal; ²Hospital de Braga, Rheumatology, Braga, Portugal; ³Unidade Local de Saúde do Alto Minho, Rheumatology, Ponte de Lima, Portugal

Background: Although spondyloarthritis (SpA) is primarily a musculoskeletal condition, ocular involvement is an important clinical feature and contributes to the burden of disease. Acute anterior uveitis (AAU) is classically described as the most frequent extra-articular manifestation of SpA and in some cases the first clinical presentation. The prevalence of AAU varies according to the sub-type of SpA. In a systematic literature review, the mean prevalence of AAU was 32.7% and a positive association between HLA-B27 positivity, axial SpA, male sex and uveitis has been reported (1). More recently, some cross-sectional studies have described lower odds of spondyloarthritis-related uveitis (SpA-U) in smokers than in patients who are ex smokers or never smokers (2). Predictors of SpA-U are poorly defined in literature and the influence of smoking status remains controversial.

Objectives: To analyse the factors associated with uveitis in SpA patients in a Tertiary Rheumatology Center.

Methods: An observational cross-sectional study was performed including patients fulfilling the ASAS criteria for axial SpA with a follow-up visit between January and June 2019. Clinical patients' charts were reviewed and the following variables were considered: age, gender, history of uveitis (confirmed by ophthalmologist observation), number of AAU episodes, smoking status (never smoker or ever smoker), HLA-B27, disease duration, disease involvement (exclusively axial or axial and peripheral), history of enthesitis and syndesmophytes. History of AAU and associated variables were determined in this subset of patients.

Statistical analysis was performed with logistic regression model. P value <.05 was defined as statistically significant.

Results: The study included 164 patients (62.3% men) with median age of 44.0 years (IQR 37 to 54) and a median disease duration of 14.6 years (IQR 9.28 to 20.32). SpA diagnosis was ankylosing spondylitis in 70.7% cases and the remaining were non-radiographic axial SpA. HLA-B27 was positive in 84.8%, 31.1% of patients were ever smokers and 21% had both axial and peripheral joint involvement. Twenty four percent of patients had at least one AAU episode. Recurrence of uveitis occurred in 70% of patients. Ever smoking (OR=2.256; 95%CI [1.077-4.276]; p<.05) and syndesmophytes (OR=2.125; 95%CI [1.009-4.475]; p<.05) showed a statistically significant association with uveitis in univariate logistic regression. Although not statistically significant, a trend to association was found between smoking and recurrence of AAU (OR=2.235; 95%CI [1.973-5.135], p=.058). In multivariate logistic regression only ever smoking was independently associated with uveitis (OR=2.542; 95%CI [1.007-6.420]; p<.05). We did not find association between presence of uveitis and gender, age, disease duration, disease involvement, HLA-B27 positivity and enthesitis.

Conclusion: Contrary to few cross-sectional studies showing a possible protective effect of smoking in SpA-U, and in line with new data from Zhao *et al* (3), we report a statistically significant independent association between history of smoking and uveitis. Nevertheless, we emphasize the need of more studies to confirm these findings.

References:

- [1] Zeboulon N, et al. Prevalence and characteristics of uveitis in the spondyloarthropathies: a systematic literature review. *Annals of Rheumatic Diseases* 2008;67:955.
- [2] Zhao S, et al. Associations between smoking and extra-axial manifestations and disease severity in axial spondyloarthritis: results from the BSR Biologics Register for Ankylosing Spondylitis (BSRBR-AS). *Rheumatology* 2018;69.
- [3] Zhao S, et al. Smoking does not protect patients with axial spondyloarthritis from attacks of uveitis. *Annals of Rheumatic Diseases* 2019;78(9).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.3802

FRI0534

PATIENT-REPORTED MEASURES OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS VARY ACROSS THE NORDIC COUNTRIES, RESULTS FROM A NORDIC COLLABORATION

B. Delcoigne¹, S. Aarrestad Provan², H. B. Hammer², D. Di Giuseppe¹, T. Frisell¹, B. Glinthorp³, G. Gröndal⁴, B. Gudbjörnsson⁵, M. L. Hetland³, B. Michelsen², D. Nordström^{6,7}, H. Relas⁷, N. Steen Krogh⁸, J. Askling¹. ¹KI, Stockholm, Sweden; ²DH Hosp., Oslo, Norway; ³DANBIO, Glostrup, Denmark; ⁴LUH, Reykjavik, Iceland; ⁵ICEBIO, Reykjavik, Iceland; ⁶UH, Helsinki, Finland; ⁷HU Hosp., Helsinki, Finland; ⁸Zitlab Aps, Frederiksberg, Denmark

Background: Disease activity in rheumatoid arthritis (RA) patients is measured through composite scores which are considered treatment targets and thus facilitate clinical decision making. Scores often combine a mix of objective and