Rheumatoid arthritis - prognosis, predictors and outcome

RHEUMATOID ARTHRITIS SEROLOGIC PHENOTYPE AT DIAGNOSIS AND SUBSEQUENT RISK FOR PNEUMONIA IDENTIFIED USING MACHINE LEARNING APPROACHES

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Background: Patients with rheumatoid arthritis (RA) are at increased risk of serious infections, with considerable excess morbidity and mortality after pneumonia. RA-related autoantibodies such as anti-cyclic citrullinated peptide (CCP) and rheumatoid factor (RF) may be generated at inflamed pulmonary mucosa prior to clinical RA onset. Therefore, patients with seropositive RA may be at increased risk for pneumonia after RA diagnosis due to subclinical pulmonary infection.

Objectives: We investigated whether seropositive RA was associated with increased pneumonia risk compared to seronegative RA.

Methods: We performed a retrospective cohort study among RA patients seen at a health care system in Boston, MA. RA patients were identified using a previously validated electronic health record (EHR) algorithm incorporating billing codes, natural language processing (NLP) of notes, medications, and laboratory results at 97% specificity. We constructed an incident RA cohort using NLP for the index date of initial mention of RA. All patients were required to have both CCP and RF data from clinical care to determine serologic RA phenotype. We used semi-supervised machine learning approaches to identify pneumonia using billing codes and terms extracted using NLP with the Center for Disease Control definition of pneumonia from medical record review as a gold standard. The area under the receiver operating curve (AUROC) for this billing code+NLP pneumonia algorithm was 0.94 compared to the standard rule-based pneumonia algorithm (billing code on inpatient discharge) AUROC of 0.86 (p=0.001). Smoking status was extracted using NLP methods. Other covariates, including a previous validated weight RA multimorbidity score, were determined using structured EHR data. We used Cox regression to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for pneumonia adjusting for potential confounders.

Results: We analyzed a total of 4,110 patients with incident RA and both CCP/RF data available. Mean age at index date was 53.0 years (SD 14.8), 77.2% were female, and 79.8% were CCP+ or RF+. During 32.24 patient-years of follow-up (mean 7.8 years/patient), we identified 240 pneumonia cases. Patients with seropositive RA had a HR of 1.99 (95% CI 1.30-3.01) for pneumonia comparing to patients with seronegative RA, adjusted for age, sex, smoking, index year, ESR level, glucocorticoid use, DMARD use, and weighted RA multimorbidity score. While CCP+ RA (HR 1.91, 95% CI 1.23-2.97) and RF+ RA (HR 2.07, 95% CI 1.35-3.16) had increased pneumonia risk compared to seronegative RA, the CCP+RF+ RA subgroup had no association with pneumonia (HR 0.67, 95% CI 0.23-1.93).

Conclusion: Patients with incident seropositive RA, particularly RF+ RA, had increased risk for pneumonia throughout the RA disease course that was not explained by measured confounders including smoking status, multimorbidity, medications, and ESR level. Further studies should investigate how RF+ may predispose RA patients to later develop pneumonia after clinical RA diagnosis.

Table. Hazard ratios for pneumonia by CCP and RF status among patients with incident RA (n=4,110).

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<th>CCP-</th>
<th>CCP+</th>
<th>RF-</th>
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<tr>
<td>CCP-</td>
<td>1.00 (Ref)</td>
<td>1.00 (Ref)</td>
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<td>CCP+</td>
<td>2.07 (1.35-3.16)</td>
<td>2.07 (1.35-3.16)</td>
<td>1.99 (1.30-3.01)</td>
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<td>RF-</td>
<td>1.91 (1.23-2.97)</td>
<td>1.91 (1.23-2.97)</td>
<td>1.99 (1.30-3.01)</td>
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<tr>
<td>RF+</td>
<td>2.07 (1.35-3.16)</td>
<td>2.07 (1.35-3.16)</td>
<td>1.99 (1.30-3.01)</td>
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References:


Acknowledgments: We thank Pfizer for financial support of this investigator initiated study. In addition we want to thank H. Hofman and W.A. ter Wee for practical study support.

Disclosure of Interests: Tomas Rusman: None declared, Mignon A.C. van der Weijden: None declared, Michael T Nurmohamed Grant/research support from: Abbvie, Bristol-Myers Squibb, Celltrion, GlaxoSmithKline, Jansen, Eli Lilly, Merck Sharp & Dohme, Mundipharma, Pfizer, Roche, Sanofi, USB, Consultant of: Abbvie, Bristol-Myers Squibb, Celltrion, GlaxoSmithKline, Jansen, Eli Lilly, Merck Sharp & Dohme, Mundipharma, Pfizer, Roche, Sanofi, USB, Speakers bureau: Abbvie, Bristol-Myers Squibb, Celltrion, GlaxoSmith-Kline, Jansen, Eli Lilly, Merck Sharp & Dohme, Mundipharma, Pfizer, Roche, Sanofi, USB, Robert B.M. Landewe Consultant of: AbbVie; AstraZeneca; Bristol-Myers Squibb; Eli Lilly & Co.; Galapagos NV; Novartis; Pfizer; UCB Pharma, Janneke J. de Winter: None declared, B.J.H. Boden: None declared, Pierre M. Bet: None declared, Camille M.A. van der Bijl: None declared, Conny J. van der Laken: None declared, Irene van der Horst-Bruinsma Grant/research support from: AbbVie; Novartis, Eli Lilly, Bristol-Myers Squibb, MSD, Pfizer, UCB Pharma, Consultant of: AbbVie, Novartis, Eli Lilly, Bristol-Myers Squibb, MSD, Pfizer, UCB Pharma

DOI: 10.1136/annrheumdis-2020-eular.3472