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Adverse Events and Persistency of Biologics in RA Patients with Interstitial Lung Disease

[1]Hanyang University Hospital for Rheumatic Diseases, [2]Clinical Research Center for Rheumatoid Arthritis (CRCRA), Seoul, [3]Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul, [4]Kyung Hee University Hospital, Seoul, [5]Ewha Womans University Mokdong Hospital, Seoul, [6]Eulji University Hospital, Daejeon, Korea

[*]Dam Kim[1,2], Soo-Kyung Cho[1,2], Soyoung Won[2], Hoon-Suk Cha[3], Chan-Bum Choi[1,2], Seung-Jae Hong[4], Jisoo Lee[5], Dong Hyuk Sheen [6], Dae-Hyun Yoo[1], Sang-Cheol Bae[1,2], Yoon-Kyoung Sung[1,2]

Objectives: We aimed to compare the incidence of adverse events (AEs) and persistency of biologics in RA patients with or without ILD. **Methods:** A total of 981 RA patients with chest radiograph or chest computed tomography (CT) data at enrollment were extracted from BIOlogics Pharmacoepidemiologic StudY (BIOPSY) cohort, a nationwide multicenter prospective cohort for biologic users of RA patients in Korea. We classified them into two groups: 1) RA-ILD group as patients with ILD, and 2) RA-non ILD group as patients without ILD. We compared the incidence of AEs during use of biologics between two groups, and then tested the differences of drug discontinuation rates due to AEs, infection, and respiratory infection between RA-ILD and RA-non ILD groups using Kaplan-Meier survival analysis and log-rank test. In addition, Cox proportional hazard model were used to identify the impact of ILD on AEs in RA patients with biologics. **Results:** The 42 patients (4.3%) revealed to have RA-ILD by chest radiograph or chest CT. Patients in RA-ILD group were older ($p<0.01$), and male patients were more in RA-ILD group ($p<0.01$). During mean follow-up of 20 months with 1,611 person years (PY), the incidence of AEs was higher in RA-ILD group (IRR 1.55, CI 1.11-2.17). In addition, the incidence of infection and respiratory infection were higher in RA-ILD group (IRR 2.38, CI 1.32-4.30 for infection, IRR 3.00, CI 1.50-5.99 for respiratory infection, respectively). The biologics discontinuation rate due to AEs was comparable in two groups ($p=0.13$), whereas the biologics discontinuation rate due to infection ($p=0.03$) and respiratory infection ($p<0.01$) were significantly higher in RA-ILD group. After adjusting for variables, age (HR 1.27, CI 1.15-1.41) and having ILD (HR 10.77, CI 2.26-51.41) were risk factors for mortality in RA patients with biologics. **Conclusions:** The incidence of adverse events, especially respiratory infections were higher in RA-ILD patients with biologics compared with RA-non ILD patients. In addition, the biologics discontinuation rate due to infection, especially respiratory infection was significantly higher in RA-ILD patients. Concerning the mortality, ILD increased the mortality in RA patients with biologics.

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Different Determination of Mortality and Cardiovascular Diseases in Rheumatoid Arthritis

[1]Division of Rheumatology, Department of Internal Medicine, Kyungpook National University

[*]Jung Su Eun[1], Eun Song Lee[1], Jong Wan Kang[1], Na Ri Kim[1], Ji Hun Kim[1], Jin Young Kang[1], Eon Jeong Nam[1], Young Mo Kang[1]

Background: Patients with rheumatoid arthritis (RA) have a higher risk of cardiovascular disease (CVD) and premature mortality, compared to the general population. Inflammatory burden and conventional cardiovascular (CV) risk factors contribute to the development of carotid atherosclerosis in RA patients. We evaluated the effects of RA on occurrence of CVD and mortality in a prospective cohort study. **Methods:** A total of 381 patients with RA and 160 healthy controls were followed up for 5 years or until deaths in the Kyungpook National University Hospital Atherosclerosis Risk in Rheumatoid Arthritis (KARRA) cohort study (417 patients and 221 controls at baseline). To detect the carotid atherosclerosis, we performed carotid ultrasound at baseline and year 5. We analyzed the incidence of CVD, conventional CV risk factors, disease activity and severity markers, mortality rate and causes of death. **Results:** During 5-year follow-up period, the mortality rate was 6.0% (25/417) in RA patients and 0% in healthy controls ($p<0.001$), while the incidence of CVD were 6.0% (25/417) in RA patients and 0.5% (1/221) in healthy controls ($p<0.001$). Among CVD in RA patients, cerebrovascular accident (CVA) and cardiovascular event (CVE) were 8 and 17 cases, respectively. Major causes of death included infection (11/25), CVD (7/25), and others (7/25). Multivariate logistic regression analysis showed that presence of carotid plaque (OR 5.80 [95% CI 1.18-28.43; $p=0.030$]), functional class (OR 4.51 [95% CI 1.51-13.51; $p=0.007$]), and ESR (OR 1.04 [95% CI 1.02-1.06; $p<0.001$]) at baseline were independent risk factor for mortality of RA patients. In contrast, carotid plaque (OR 7.20 [95% CI 1.94-26.75; $p=0.003$]) and two or more CV risk factors (OR 6.47 [95% CI 1.14-36.75; $p=0.035$]) at baseline were independent predictive factors for new-onset CVD of RA patients in a multivariate logistic regression analysis. **Conclusions:** This prospective study shows that a common risk factor for CVD and mortality is carotid plaque which is determined by disease activity and CV risk factors. While disease activity of RA is a critical determinant for the mortality, the development of CVD depends on conventional CV risk factors.