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Methotrexate and rheumatoid arthritis associated interstitial lung disease

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ABSTRACT

Question addressed by the study: Methotrexate (MTX) is a key anchor drug for rheumatoid arthritis (RA) management. Fibrotic interstitial lung disease (ILD) is a common complication of RA. Whether MTX exposure increases the risk of ILD in patients with RA is disputed. We aimed to evaluate the association of prior MTX use with development of RA-ILD.

Methods: Through a case–control study design with discovery and international replication samples, we examined the association of MTX exposure with ILD in 410 patients with chronic fibrotic ILD associated with RA (RA-ILD) and 673 patients with RA without ILD. Estimates were pooled over the different samples using meta-analysis techniques.

Results: Analysis of the discovery sample revealed an inverse relationship between MTX exposure and RA-ILD (adjusted OR 0.46, 95% CI 0.24–0.90; p=0.022), which was confirmed in the replication samples (pooled adjusted OR 0.39, 95% CI 0.19–0.79; p=0.009). The combined estimate using both the derivation and validation samples revealed an adjusted OR of 0.43 (95% CI 0.26–0.69; p=0.0006). MTX ever-users were less frequent among patients with RA-ILD compared to those without ILD, irrespective of chest high-resolution computed tomography pattern. In patients with RA-ILD, ILD detection was significantly delayed in MTX ever-users compared to never-users (11.4±10.4 years and 4.0±7.4 years, respectively; p<0.001).

Answer to the question: Our results suggest that MTX use is not associated with an increased risk of RA-ILD in patients with RA, and that ILD was detected later in MTX-treated patients.