Master: Epidemiology (2nd Edition)

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ABSTRACT

INTRODUCTION: Chronic inflammatory diseases, such as Rheumatoid Arthritis (RA) lead to increases in systemic markers of inflammation such as C-reactive protein, TNF and IL6, among others, which may predispose to the development of both insulin resistance and Type 2 Diabetes Mellitus (T2DM). Thus, a relevant question is if the risk of T2DM is increased in patients with RA.

OBJECTIVES: We aimed to compare incidence rates of self-reported T2DM in RA versus non-RA populations and study the influence of cardiovascular risk factors and RA drugs on those rates.

METHODS: The study population consisted of participants in the National Data Bank for Rheumatic Diseases (NDB), a longitudinal outcomes research study on rheumatologic disorders, where patients complete semiannual questionnaires that document events in the preceding 6 months, from 1998 through 2008. All subjects were free from the outcome under investigation at the beginning of followup. Osteoarthritis (OA) patients were used as controls. T2DM was determined based on self-reports of disease and on the use of hypoglycemic medication. The association between RA and T2DM was investigated using COX logistic regressions adjusted for several relevant clinical and demographic covariates.

RESULTS: A total of 14,481 participants diagnosed with RA (79.5% female; mean age 58.1 years) and 3,441 participants diagnosed with OA (84.5% female; mean age 63.6 years) were followed during 69,943 person-years. RA subjects were significantly younger, had a lower Body Mass Index (BMI) and less major comorbidities than controls. RA patients were less likely to have graduated from high school (p<0.001). In patients with RA the T2DM incidence rate was 10 per 1000 person-years, while the incidence rate for OA was 15 per 1000 person-years. Both rates are superior to most estimates calculated among the US population. The covariate-adjusted risk of T2DM in patients with RA versus OA was not significant (HR=0.94; 95% CI: 0.79-1.12, p=NS). Male gender, age, non-caucasian ethnicity, major comorbidities, low education level, prednisone intake, and higher BMI were significantly associated with the incidence of T2DM. On the other hand, RA drugs had a clear protective role on TDM2, mainly methotrexate (19% risk reduction; p=0.022) and hydroxicloroquine (47% risk reduction; p<0.001).

CONCLUSION: To our knowledge, this is the largest study dedicated to the association of RA and T2DM. Our results suggest that RA *per se* is not associated with increased risk of T2DM. Both RA and OA are associated with known TDM2 risk factors, such as BMI and number of comorbidities, increasing the incidence rates of TDM2. Some of the drugs used in RA treatment seem to have a significant protective effect on the TDM2 risk.

Key Words: Rheumatoid Arthritis; Type 2 Diabetes Mellitus; Osteoarthritis; Methotrexate; Hydroxicloroquine.