中文題目：僵直性脊椎炎病人與重大心血管事件風險之全國性研究

英文題目：Factors Associated with Risk of Major Adverse Cardiovascular Events in Treated Ankylosing Spondylitis Patients

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Background: Ankylosing spondylitis (AS) is a chronic, systemic autoinflammatory disease typically characterized by axial spondyloarthritis, sacroiliitis, and enthesitis. The main medical management includes use of long-term non-steroidal anti-inflammatory drugs (NSAIDs) and conventional synthetic disease-modifying antirheumatic Drugs (csDMARDs), such as methotrexate and sulfasalazine. Some biologics indicated for advanced AS are also developing. With long-term use of various NSAIDs, patients with AS are at higher risk for cardiovascular diseases. Development of a predictive algorithm for risk of major adverse cardiovascular events (MACE) in AS patients based on identified risk factors is a clinical necessity for a better management. The related epidemiologic studies are still lacking currently. We thus aim to investigate factors associated with MACE in patients with incident AS requiring medical therapy.

Methods: We conducted a nationwide case-control study using the 2003–2013 Taiwan National Health Insurance Research Database. From 2004 to 2012, we identified 42,595 newly-diagnosed AS patients requiring medical therapy without previous MACE (myocardial infarction, ischemic stroke, or patients who underwent coronary artery bypass graft or percutaneous coronary intervention), of whom 1,151 patients (2.7%) developed MACE during the follow-up period. We matched MACE cases with patients without MACE at a 1:4 ratio for age, gender, disease duration and year of MACE diagnosis date (index date), and finally included 947 MACE cases and 3,896 non-MACE matched controls for analyses. We examined the associations of MACE with low income, urbanization, extra-articular manifestations (i.e., acute anterior uveitis [AAU], psoriasis and inflammatory bowel disease [IBD]), comorbidities, use of biological agents, sulfasalazine use, methotrexate use, the daily dosage of corticosteroids, and the cumulative defined daily dose (DDD) of NSAIDs categorized by traditional NSAIDs, selective cyclooxygenase-2 inhibitors (COX-2i) and preferential COX-2i within one year before the index date using conditional logistic regression analyses shown as adjusted odds ratio (aOR) with 95% confidence

intervals (CIs).

Results: The risk of MACE was associated with the use of corticosteroids in a dose-dependent manner (prednisolone equivalent dose < 5 mg/day: aOR, 1.25; 95% CI, 1.02-1.54, p = 0.031; ≥ 5 mg/day: aOR, 4.76; 95% CI, 3.51-6.46, p < 0.001), use of traditional NSAIDs with 7.75–21 DDDs (aOR, 1.39; 95% CI, 1.05-1.85, p = 0.023) within one year, and use of selective COX-2i with ≤ 28 DDDs (aOR, 1.37; 95% CI, 1.02-1.85, p = 0.036) or > 132 DDDs (aOR, 1.61; 95% CI, 1.12-2.32, p = 0.011) within one year. Use of biological agents tended to decrease the risk of MACE (aOR, 0.35; 95%CI, 0.12-1.03; p = 0.056). Other risk factors for MACE development included residence in rural region (aOR, 1.31; 95% CI, 1.03–1.68, p = 0.031), comorbidities including hypertension (aOR, 3.14; 95% CI, 2.58-3.82, p < 0.001), hyperlipidemia (aOR, 5.01; 95% CI, 4.14-6.04, p < 0.001), diabetes mellitus (aOR, 1.69; 95% CI, 1.37-2.08, p < 0.001), chronic kidney disease (aOR, 2.00; 95% CI, 1.36-2.94, p < 0.001), heart failure (aOR, 4.06; 95% CI, 2.76-5.99, p < 0.001), and valvular heart disease (aOR, 2.03; 95% CI, 1.30-3.15, p = 0.002). However, low income, extra-articular manifestations, methotrexate use, sulfasalazine use and use of preferential COX-2i were not associated with the development of MACE.

Conclusions: This nationwide, population-based study showed that significant risk factors for MACE development in AS patients included residence in rural region, hypertension, hyperlipidemia, diabetes mellitus, chronic kidney disease, heart failure, valvular heart disease, use of corticosteroids in a dose-dependent manner, use of traditional NSAIDs with 7.75–21 DDDs within one year, and use of selective COX-2i with ≤ 28 DDDs or >132 DDDs within one year.