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Letter

Questions on the Bidirectional Relationship Between Primary Sjögren Syndrome and Non-Hodgkin Lymphoma

To the Editor:

We have read with great interest in the article by Wang, *et al* on the higher incidence of non-Hodgkin lymphoma (NHL) in patients with primary Sjögren syndrome (pSS) and the higher incidence of pSS in patients with NHL[1]. Thank you for the discovery of the bilateral relationship between pSS and NHL in this nationwide population-based study[1]. However, we have some questions and findings that we would like to discuss.

First, although the pSS cohort excluded patients diagnosed with other specific autoimmune diseases before the index date, it was hard to identify if there were patients who had other autoimmune diseases diagnosed during the study period, from the date of application date for a catastrophic illness certificate (CIC) of pSS in patients with pSS until NHL was diagnosed. In addition, there was a possibility of underdiagnosis of other specific autoimmune diseases before the index date that may influence the incidence of NHL in patients with pSS, since other specific autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus) are consistently reported for increasing NHL risks, and it is common for pSS to be combined with other autoimmune diseases[2]. Except for the confounders mentioned above, obesity and immunocompromised patients (e.g., HIV/AIDS and organ transplantation) were also potential risk factors of NHL[3]. All prominent confounders including those that Wang, *et al* indicated in the discussion[1] such as smoking habit[4], family history[5], specific virus or bacterial infections, and other confounders referred to in this letter that may influence incidence rate of pSS and NHL[3,6] should all be adjusted to make the data of this study more accurate and reliable.

Second, there may be a delay in the CIC application, and the interval between the diagnostic date and the CIC application date should be taken into consideration. Patients may have had the diagnosis of pSS long before they received the CIC.

Third, in both the pSS and NHL cohorts, the treatments for the diseases were not taken into consideration. The treatments for pSS (e.g., some disease-modifying antirheumatic drugs, nonsteroidal antiinflammatory drugs, systemic corticosteroids) may potentially increase the incidence of NHL in patients with pSS and vice versa[7]; the treatments for NHL may also affect the incidence of pSS in patients with NHL. For example, rituximab can be administered for both NHL and pSS[8]. Further, assessment of disease severity and treatments may better predict the relationship between NHL and pSS[8].

If the questions mentioned in correspondence could be further clarified, this study could become more representative and complete.

Yun-Tzu Liang[1]
Pui-Ying Leong[2,3], MD
James Cheng-Chung Wei[2,3,4], MD, PhD
[1]School of Medicine, Chung Shan Medical University;
[2]Department of Allergy, Immunology and Rheumatology, Chung Shan Medical University Hospital;
[3]Institute of Medicine, Chung Shan Medical University;
[4]Graduate Institute of Integrated Medicine, China Medical University, Taichung, Taiwan.

Y.T. Liang and P.Y. Leong contributed equally to this article.

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Address correspondence to Dr. J.C. Wei, Department of Allergy, Immunology and Rheumatology, Chung Shan Medical University, No. 110, Sec. 1, Jianguo N. Rd., South District, Taichung City 40201, Taiwan. Email: jccwei@gmail.com.

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