Response to: 'Comment on Ye *et al* 'Presence of respiratory failure of COVID-19 infection in patients with rheumatism in Wuhan, China" by Chen *et al*

We appreciate the valuable comments from Chen *et al* on our recent study about the clinical characteristics of COVID-19 cases with rheumatic disease.[1] They highlight an important point about the sample size of patients with rheumatism infected with COVID-19 in our study. We agree that the sample size was relatively small, although we have included all such cases in Tongji Hospital, the hospital that admitted the most patients with COVID-19 in China. We acknowledged this limitation in the discussion of the paper.[2] With the urgent pandemic of COVID-19, the aim of this study is to provide a timely report to present the clinical features of patients with rheumatism infected with COVID-19. The clinical manifestation of COVID-19 cases with rheumatic disease in Wuhan, the first COVID-19 epicentre in the world, may provide important information for disease management in patients with rheumatic disease in other areas of the world. In our report, we noticed that respiratory failure was more common in patients with rheumatism (38% vs 10%, p<0.001) infected with COVID-19, although the duration of hospital stay and mortality were similar between patients with rheumatic disease and those without rheumatic disease.[2] These results were confirmed by subsequent studies in other areas of the world.[3 4] An analysis of COVID-19 cases in Massachusetts, USA showed that there were higher rates of intensive care admission and mechanical ventilation, but not mortality, in patients with rheumatism infected with COVID-19, compared with those without rheumatic disease (48% vs 18%; OR: 3.11, 95% CI: 1.07 to 9.05, p=0.01).[3] Fredi *et al* also reported that patients with rheumatism infected with COVID-19 in northern Italy tend to be treated more often with high-dose glucocorticoids (65% vs 48%, p=0.14) and tocilizumab (23% vs 18%, p=0.55), due to the 'worsening of respiratory condition'.[4]

Regarding the effects of antirheumatic drugs, we agree that different disease and different medication may have different effects on disease condition. Due to the limited sample size, we did not subcategorise the patients into different groups based on different rheumatic disease or use of different disease-modifying antirheumatic drugs (DMARDs) when analysing some parameters. Although the use of high-dose glucocorticoids and chloroquine/hydroxychloroquine as a therapeutic approach in patients with COVID-19 is controversial, whether their use in patients with rheumatic disease as an antirheumatic medication (usually at lower doses and in a long-term manner) could affect COVID-19 susceptibility and severity remains elusive. By including 600 cases with rheumatic disease and COVID-19 from 40 countries, Gianfrancesco *et al* reported that use of tumour necrosis factor inhibitor was associated with a lower hospitalisation rate.[5] In contrast, use of non-steroidal anti-inflammatory drugs or conventional DMARDs was not associated with hospitalisation.[5] However, the effects of DMARDs use on other clinical characteristics of COVID-19 are not completely understood. We currently continue collecting data from other centres in Hubei province, aiming to increase the sample size and investigate the potential effects of DMARDs on COVID-19 using a larger dataset in Hubei, China.

Chen *et al* also raised an important point of missing values for some parameters in figure 3. We agree that the reasons for these missing data may due to the fact that clinicians may not see the need for certain tests or the patients' conditions may prevent certain tests. In Figure 3 of our study, the tests, such as white blood cell (WBC) count, lymphocyte count, neutrophil count, platelet count, haemoglobin, alanine aminotransferase, aspartate aminotransferase, direct and total bilirubin, creatinine, uric acid, activated partial thromboplastin time, prothrombin time, fibrinogen, high-sensitivity C-reactive protein and procalcitonin, had data from all patients. We found that leucopenia was rarely seen in patients with rheumatic disease (5%), despite the fact that lymphopenia was more common (57%). D'Silva *et al* reported similar findings in a recent study.[3] While WBC count in patients with rheumatism infected with COVID-19 was higher than that in those without rheumatic disease, lymphocyte count was similar in both the groups.[3] However, there were a few missing values in some tests including creatine kinase (CK, missing eight values) and cardiac troponin I (cTn-I, missing one value) in our study. We noticed in our study that the patients, who had highest level of CK (1248 U/L) and cTn-I (124.8 pg/mL), eventually passed away. An earlier report on patients with COVID-19 in Wuhan has indicated that deceased patients with COVID-19 had higher levels of cTn-I (22.2 vs 3.0 pg/mL, p<0.0001) and CK (39.0 vs 18.0 U/L, p<0.0001), compared with survivors.[6] These results suggest that clinicians should pay close attention to the injury of other organs. However, we agree that it requires further investigation to confirm the value of these parameters in determining the prognosis of COVID-19 in patients with rheumatism.

Due to the immunosuppressive effect of a number of antirheumatic drugs and the immune dysregulation underlying rheumatic diseases, patients with rheumatic disease have received great attention during the pandemic of COVID-19.[7] As the first epicentre of COVID-19 in the world, the clinical data of COVID-19 cases with rheumatic disease may provide first-hand information for the clinical practice of rheumatologists during the pandemic. With the rapid increase in the number of COVID-19 cases, there will be more investigations to supplement and revise our findings in patients with rheumatism infected with COVID-19.

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