Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

decision to start a 5-day intravenous infusion of iloprost was based on an expert clinical diagnosis of digital ischaemia by the treating consultant and a persistent oxygen requirement that probably reflected systemic microvasculopathy.

After a continuous 5-day infusion of 0·5 mg/kg per min, we noted a sustained clinical improvement in the digital ischaemia, as well as in cardiovascular and respiratory parameters. In all patients, decreasing oxygen requirements, increasing PaO_2:FiO_2 ratio, and normalisation of heart rate were seen up to 48 h after the cessation of the iloprost infusion (appendix p 3). None of the patients required mechanical ventilation during their hospital admission and all tolerated the iloprost infusion well with no bleeding complications or serious adverse events to warrant cessation. One patient had diarrhoea during the infusion that terminated upon iloprost withdrawal. Notably, upon cessation of iloprost on day 5, a mild rebound tachycardia and transient worsening of symptoms was observed, but these issues resolved without further treatment before discharge in all patients. One patient's hospital course was complicated by a pulmonary embolus that required a longer stay, but the patient remained stable and was discharged on rivaroxaban.

This case series illustrates that iloprost might be a useful adjunctive therapy for COVID-19 vasculopathy, improving digital ischaemia as well as cardiorespiratory parameters. Inhaled iloprost has been shown to improve ventilation parameters through its vasodilatory effects, thereby improving gas exchange.[10] Furthermore, systemically infused iloprost might also improve ventilation and perfusion matching in the lung, leading to the effects observed in our patients. Although larger controlled studies are needed to confirm our observations and despite the limitations inherent to small case series, based on the pharmacological effects of iloprost in analogous pathological states and its favourable safety profile, we suggest that iloprost might be a useful adjunctive treatment in COVID-19.

We declare no competing interests. The Royal Free Hospital Ethics board committee approved this study. All patients provided written and verbal informed consent for treatment and publication.

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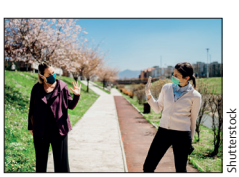
Patients with rheumatic diseases adhere to COVID-19 isolation measures more strictly than the general population

There is a continuous debate about the risks of increased incidence of COVID-19 in vulnerable patient groups, which includes patients with rheumatic diseases and especially those treated with immunosuppressive antirheumatic drugs, including biologics. So far, results on the incidence and the outcomes of COVID-19 in these groups are reassuring: to date, neither presence of a rheumatic disease nor use of immunosuppressive medication have shown associations with higher infection rates or worse disease course of COVID-19.[1–5] However, these studies do not account for preventive measures taken by patients, despite suggestions that patients are aware that their infection risk might be increased.[1,4,5] If patients subject themselves to stricter isolation measures than the general population, we might be falsely reassured. In this study, we compared the isolation measures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taken by patients with rheumatic disease and healthy participants.

See Online for appendix

These are the first results of an ongoing prospective cohort study in patients with rheumatic disease and a healthy control group (Netherlands Trial Register, trial ID NL8513). During the first wave of COVID-19 in the Netherlands, all adult patients with rheumatoid arthritis, ankylosing spondylitis, or psoriatic arthritis from the Amsterdam Rheumatology and Immunology Center (Reade, Amsterdam, Netherlands) were invited to participate in this study. All patients were asked (but not obliged) to register a control participant from their family or close network who did not have a rheumatic disease, was the same sex, and was of a similar age (<5 years difference). Information on demographic data, medication use, rheumatic disease activity, COVID-19-related complaints, and implementation of self-isolation measures was collected with questionnaires administered online. The results of the first questionnaire were used to analyse to what extent patients with rheumatic disease adhere to isolation measures compared with controls. In the questionnaire, patients were able to choose between five categories: no measures at all, only hygiene measures (washing hands more frequently), hygiene measures and physical distancing (keeping 1·5 m distance from other people as per Dutch guidelines), all aforementioned measures and staying indoors as much as possible, or total isolation. A distinction was made between strict and mild isolation measures. Mild isolation measures were defined as adherence to only hygiene measures or phsyical distancing. Strict isolation was defined as staying indoors as much as possible and complete social isolation. All patients were included in the analyses. Multivariable logistic regression analysed the differences in isolation measures between patients and controls. Associations were adjusted for sex, age, body-mass index, smoking status, and the presence of comorbidities. A threshold of p<0·05 was used for interaction terms for the identification of effect modifiers. All subgroup analyses were exploratory, so no correction was applied for multiple testing. SPSS version 23.0 was used for the analyses. The research protocol was approved by the medical ethical committee of the VU University Medical Center (registration number 2020.169), and all participants gave written informed consent.

Between April 26, 2020, and May 27, 2020, 979 consecutive patients with rheumatoid arthritis, 215 patients with ankylosing spondylitis, 261 patients with psoriatic arthritis, and 414 consecutive healthy controls were included in this study (appendix p 1). Demographic characteristics were as expected in these populations (appendix p 2), but unfortunately the control group was much smaller than the patient group and not completely matched. 877 (60%) of 1455 patients were on treatment with conventional disease-modifying anti-rheumatic drugs (DMARDs). The majority of patients with rheumatoid arthritis (595 [61%] of 979) and patients with psoriatic arthritis (135 [52%] of 261) were on methotrexate, compared with a minority of patients with ankylosing spondylitis (six [3%] of 215). In addition, 646 (44%) of 1455 patients were receiving biological DMARDs, most of which were tumour necrosis factor inhibitors (563 [39%] of 1455 patients overall, 336 [34%] of 979 patients with rheumatoid arthritis, 106 [49%] of 215 of patients with ankylosing spondylitis, and 121 [46%] of 261 patients with psoriatic arthritis).

During this study, the Dutch Government encouraged the general population to stay indoors as much as possible and to keep 1·5 m distance from each other. 666 (46%) patients adhered to strict isolation measures (448 [46%] of 979 patients with rheumatoid arthritis, 98 [46%] of 215 patients with ankylosing spondylitis, and 120 [46%] of 261 patients with psoriatic arthritis), compared with 122 (29%) healthy controls (appendix p 2). After adjusting for age, sex, smoking status, body-mass index, and presence of comorbidities, patients were almost twice as likely to adhere to strict isolation measures compared with healthy controls (odds ratio [OR] 1·8, 95% CI 1·5–2·4, p<0·01). This association remained significant for all disease subgroups compared with controls (appendix p 3).

Sex was found to be a significant effect modifier (appendix p 3): preference for strict isolation was higher in women than in men. In patients with rheumatic disease, those receiving biological DMARDs took stricter isolation measures than patients not receiving biological DMARDs (OR 1·3, 95% CI 1·1–1·7; p=0·02; appendix p 3).

A limitation of this study was that the control participants were neither a random population sample nor a perfect match for the patients with rheumatic disease, obviating a clean comparison. We tried to correct for this by adjusting for a set of potential confounders.

The observation that the presence of a rheumatic disease and use of immunosuppressive medication are

not associated with a higher incidence or worse disease outcome of COVID-19[1–5] might thus, in whole or in part, be caused by strict isolation measures taken by individual patients with inflammatory rheumatic diseases such as rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis, and especially those receiving biological DMARDs with potential extra risk. This phenomenon might occur in other vulnerable patient groups as well. Therefore, the assessment of risk of COVID-19 in vulnerable patients should include an evaluation of isolation measures they have actually taken.

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