

Title: Adopting PROs in virtual and outpatient management of RA.

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Standfirst

As the coronavirus pandemic has catalysed the sudden adoption of telemedicine in management of rheumatoid arthritis, the RAID patient reported outcome may help identify patients best suited to telemedicine review and also promote holistic management of subjective symptoms that might otherwise be overlooked when only treating to disease activity targets.

Main text

Darwin famously adhered to the principle “*natura non facit saltus*”, that “nature does not make leaps”, proposing that evolution proceeds in a stepwise manner. However, contemporary palaeontologists have challenged this viewpoint, interpreting the fossil record as showing long periods of stasis with episodic acceleration in speciation, perhaps catalysed by environmental change. And as I pick up a beautifully formed fossil brachiopod in Oxfordshire while dog walking during the SARS-Cov-2 lockdown, it occurs to me that the unprecedented circumstances of this coronavirus pandemic might similarly catalyse a major change in otherwise long-established rheumatology practices.

The sudden emergence of SARS-Cov-2 on the world stage, and the high morbidity and mortality associated with COVID-19 symptoms in a proportion of those infected, has accelerated a major change in the management of our patients with rheumatoid arthritis (RA) and in particular, the rapid emergence of telemedicine.

The ideal immunological goal of management is to correct the immune dysregulation that characterises RA, causing joint destruction and systemic comorbidity, and to restore immune homeostasis. And in doing so, the hope is that subjective symptomatology accompanying RA will correspondingly resolve. But in the absence of biomarkers that reliably inform management decisions, the accepted paradigm is to treat to a target of remission or low disease activity, as assessed by composite scores of disease activity, and to titrate therapy according to response. However, in the context of a pandemic, rheumatologists must be mindful that many of the pharmacological interventions in the now substantial armamentarium are potentially immunosuppressive and may therefore increase risk of viral contagion. Conversely, it has emerged that the pathobiology of COVID-19 mortality is related to exaggerated host immune responses and for this reason, several rheumatology drugs that target cytokines are being investigated as potential treatments in people with severe COVID-19 related pathology.

In the face of the SARS-Cov-2 pandemic, rheumatologists have stratified the risk to people with RA according to their treatment regime, age, and comorbidities. But at the same time, the importance of maintaining “tight control” of inflammation has been emphasised with a view to minimising the risks associated with inadequately treated RA and in the knowledge that poorly controlled disease is in itself a risk factor for serious infectious complications. Abundant evidence from many clinical studies demonstrate the effectiveness of a continuous goal-oriented treat-to-target approach with respect to improved and maintained clinical, functional, and radiographic outcomes¹. At a group level, patient-reported outcomes also improve. However, the aspirational target of sustained remission or, failing that, low disease activity, is not attainable for many individuals. And furthermore, among those who do achieve the therapeutic target, subjective symptoms may remain. Prominent among these are pain, fatigue, and functional loss². As these symptoms are known only to the patient themselves, they may be overlooked when treating to a disease activity target.

In a sudden transition of practice to telemedicine, can patient-reported outcomes (PROs) help ensure that we continue to achieve optimum disease control and address the concerns of people living with RA in a more holistic manner? The recent publication by Mistry et al suggest that this might be the case, at least for carefully selected patients³. The group from St George’s NHS foundation Trust in London assessed the performance of the Rheumatoid Arthritis Impact of Disease

(RAID) PRO instrument relative to the Disease Activity Score with 28-joint count (DAS28) in a cohort of people with established RA. RAID was developed as a EULAR initiative to combine the most important PROs into one measure⁴. It comprises seven domains encompassing pain, fatigue, physical function, sleep, physical and emotional well-being, and coping. Each domain is scored using a numeric rating scale, giving a total score of 0–10, with higher scores indicating greater disease impact. A RAID score of <2 is regarded as a Patient Acceptable Symptom State (PASS)⁵. PASS is another PRO defined as a symptom state that the patient considers acceptable. It recognizes that patients consider feeling good to be more important than feeling better⁶. The researchers from St. George's hospital noted that patients reported no difficulties understanding or completing the RAID questions, which can be done in advance of the consultation and take less than 5 minutes. RAID scores correlated strongly with DAS28-ESR, DAS28-CRP and with the patient global assessment (PGA) component of the composite score. Of note, the PGA covers two concepts: global health and overall disease activity and is the PRO incorporated into most of the ACR- and EULAR-endorsed RA assessment tools. Although PGA is included in the DAS28, its weighting is low, so that it has relatively little influence on the final DAS28 score.

The relationship between each subcomponent of the DAS28 and the RAID score was explored using mixed-effects linear regression. Mistry et al found both the patient global VAS and the square root TJC to be highly statistically significantly associated with RAID scores ($P < 0.01$)³. Importantly, of 66/198 patients with a RAID score <2, between 92%–97% met remission criteria and 98.5% were in remission or low disease activity by DAS28-ESR or DAS28-CRP thresholds. These data give considerable confidence that in a telemedicine setting, patients reporting RAID <2 would have attained a DAS28 treat-to-target goal. Conversely, of 134 patients in low disease activity or remission, RAID was ≥ 2 in 51.5%. This high proportion of patients with symptomatology in the unacceptable range, despite meeting contemporary disease activity treatment targets, cautions against over-reliance on protocol driven medicine in the outpatient clinic and emphasises the value of PROs used adjunctively to composite scores of disease activity⁷. The RAID domains with the largest proportion of subjects in the severe range (7–10) were fatigue 35.6%, sleep 33.3%, and emotional well-being 28.9%. In the context of outpatient clinic consultations, inspection of scores across the RAID domains may help quickly identify key unmet needs for an individual who has attained the disease activity treatment target. And in doing so, initiate beneficial, non-pharmacological management approaches such as lifestyle advice and cognitive behavioural therapy, both of which could be amenable to telemedicine delivery.

A good therapeutic goal from the perspective of a patient is “to have a good day”⁸. The evidence suggests that RAID can assist in shared decision making, whether in an outpatient clinic or telemedicine setting, to achieve this. RAID could also be used to triage those patients best suited to telemedicine follow up. As expressed so well by Sir William Osler, rheumatologists should be mindful that “the good physician treats the disease, but the great physician treats the patient who has the disease”⁹.

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Competing interests

None