

# Orthopaedic long COVID - the unknown unknowns

## ARE WE FACING A PANDEMIC OF AVASCULAR NECROSIS FOLLOWING COVID-19?



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The world has been locked in a duel with the SARS-CoV-2 virus. The ensuing COVID-19 pandemic has led to previously unthinkable changes, not only to how healthcare systems function, but also the demands placed upon those systems.<sup>1,2</sup> From an orthopaedic perspective, elective operations for those suffering with what are often severe, life-limiting conditions were cancelled to allow health services to cope with the successive waves of COVID-19 patients.<sup>3</sup> This has resulted in a staggering increase in waiting lists to levels that will take years to bring back under control.<sup>4</sup> It has also resulted in twice the number of patients who are waiting for total hip or knee arthroplasty experiencing a state of life which can be considered as “worse than death”.<sup>5</sup>

In a Rumsfeldian matrix, when emerging from this pandemic, the burden of degenerative joint disease can largely be thought of as our “known knowns”. However, we must not forget that there are also unknown unknowns. COVID-19 has caused repeated anguish to medical services, not only in the management of the disease itself but also in the long-term effects of the virus and its treatment. Chronic symptoms of fatigue, headaches, and dyspnoea are just some of the unexpected consequences which medical professionals have begun to recognize in those who have recovered.<sup>6</sup>

Other unforeseen consequences may well be found as a result of the drug treatments used to combat the effects of the disease. Glucocorticoids have been used to manage acute respiratory disease syndrome (ARDS) in COVID-19 patients, and have shown to be beneficial in reducing 28-day mortality and the need for mechanical ventilation.<sup>7,8</sup> Ostensibly effective in the treatment of ARDS, the widespread use of such treatment may be a double-edged sword.

The detrimental effects of steroids are well documented, and the link between these drugs and the occurrence of femoral head avascular necrosis (AVN) is increasingly recognized.<sup>9,10</sup> AVN involves progressive destruction of bone as a result of compromise of bone vasculature,<sup>11,12</sup> death of osteocytes and fat cells, and alteration of bone architecture. Following the SARS epidemic in 2003, high rates of femoral head AVN (up to 23%) were noted in patients recovering from the condition who had received steroid treatment.<sup>13</sup> The link between COVID-19 and AVN in those who have received steroids has been reported.<sup>14</sup> If the rates of AVN reach the heights of those reported following SARS, then orthopaedic services may be subject to a pandemic of AVN, and result in a significant increase in the burden of musculoskeletal disease in the community.

The use of steroid medications and their relationship to AVN have been previously shown to be related to cumulative dose.<sup>15</sup> Many COVID-19 patients are started on glucocorticoid medications when they show signs of respiratory deterioration. Dosing of 6 mg dexamethasone daily for ten days was shown by the RECOVERY group to reduce 28-day mortality and the need for mechanical ventilation.<sup>8</sup> This dose regime is well below the cumulative dose thresholds described in much of the literature (cumulative dose of 2,000mg prednisone or its equivalent), but this fact does little to mollify concerns.<sup>16,17</sup> AVN has however been described at much lower dose thresholds; furthermore, COVID-19 may independently predispose patients to developing the condition.<sup>18,19</sup> Larger steroid doses are commonly used if patients deteriorate or are admitted to critical care, with such patients receiving much higher doses than those used in the RECOVERY trial.<sup>20</sup>

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Many of those affected by AVN of the femoral head are young and active, which makes the management of such a potentially devastating condition troublesome. Treatment options in advanced disease are limited and even though there are a few novel treatments under investigation,<sup>21,22</sup> effective joint-preserving treatment relies on early diagnosis. The mainstay of diagnosis is MRI, and it has been shown to be effective in the identification of AVN in asymptomatic high-risk patients. It is not, however, full-proof, with Zhao et al<sup>23</sup> showing that there is a significant risk of failing to identify the condition if a single scan conducted two to three months following the insult is relied upon for diagnosis. Despite improvements in joint-preserving procedures, many young patients are managed with arthroplasty surgery, particularly when diagnosed late.<sup>24-26</sup>

The long-term consequences of the COVID-19 pandemic and its effect on both individuals and wider healthcare systems should be cautiously considered. If the previous experience with SARS and its relationship to subsequent AVN is observed following the current pandemic, then the life-altering effect of AVN on countless individuals will have ramifications for orthopaedic services. An awareness of the possible orthopaedic ramifications of the disease – ‘orthopaedic long COVID’ – is therefore vital for all medical professionals dealing with patients convalescing following COVID-19.

## Twitter

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