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*Original Article*

# Musculoskeletal corticosteroid injections were used safely in patients during the COVID-19 pandemic

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## ABSTRACT

**Objectives:** Studies have highlighted that corticosteroid use can cause immunocompromise. During the COVID-19 pandemic, caution was advised on corticosteroid injections (CSIs) use and the possibility of increasing patients' susceptibility to COVID-19. CSI is commonly used to manage pain, which is increasingly important with prolonged waiting lists. This study aimed to assess the occurrence of COVID-19 infection following the administration of CSI for musculoskeletal pain.

**Methods:** A prospective cohort study of patients receiving CSI for musculoskeletal conditions through the COVID-19 pandemic was followed. It monitored post-injection through clinical review and telephone follow-up as to whether they were diagnosed with COVID-19 or had its symptoms. Patients were administered either half or full-dose corticosteroids as per guidance at the time. Patients were followed up at 8 weeks, 3 and 6 months.

**Results:** One hundred and ninety-six patients were included (100 males and 96 females). One hundred and fourteen patients received 40 mg of Depo-Medrone, and 90 received 20 mg of Depo-Medrone. No patients suffered COVID-19 symptoms or had positive viral polymerase chain reaction (PCR) tests by 3-month follow-up. By the 6-month follow-up, four of the cohort had mild symptoms and a positive PCR test for COVID-19. None required hospitalization.

**Conclusion:** Our study demonstrated only a 2% incidence of COVID-19 infection following the administration of CSI for musculoskeletal pain within the 6-month follow-up, despite a high local prevalence for infection. We observed no correlation between CSI and COVID-19 acquisition and noted no clear increase in risk. We would therefore endorse CSI use if required for patients after careful patient selection and shared decision-making.

**Keywords:** COVID-19, Corticosteroid, Injections, Musculoskeletal, Pain

## INTRODUCTION

Throughout the global COVID-19 pandemic, waiting lists have been increasing;[1] and while the priority has been to minimize the impact of the pandemic, patients have still been presenting and requiring management for chronic illnesses.

Musculoskeletal pain can be debilitating and encompasses a wide range of disease processes.[2] Musculoskeletal corticosteroid injections (CSIs) are common procedures, often performed in elective orthopedic or rheumatology clinics. The injection is often used as a part of an analgesic

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ladder to aid in treating a variety of musculoskeletal pathologies, such as arthritic joint pain, bursitis, tendinopathy, and joint inflammation.[3] Many studies demonstrate that CSI helps patients control joint pain, improves their quality of life, provides a better range of movement, facilitates returning to work sooner and, in certain patients, may help to delay or prevent operative intervention.[4] CSI is a safe procedure with a small risk of complications.[4]

CSI can also be used as a diagnostic test. It is generally considered good practice for a patient to be offered or receive a CSI before committing them to the more invasive treatment of musculoskeletal surgery. However, there has long been discussion about whether using CSI increases a patient's susceptibility to contracting viral illnesses.[5] During the COVID-19 pandemic, multiple societies,[6] including the British Orthopaedic Association, issued caution statements for the use of CSI in patients and to stress the impact it could have on patients' susceptibility to contracting COVID-19.[7,8]

Systemic exogenous corticosteroids act similarly to endogenous corticosteroids and therefore possess similar actions and side effects. They suppress both the innate and adaptive immune systems, leading to a wide range of physiological consequences, including a reduced immune response and susceptibility to infection.[9,10] These effects include reducing cortisol, suppressing the hypothalamic-pituitary-adrenal axis, and significantly decreasing inflammatory cytokines.[11] With this in mind, it has been previously demonstrated that intra-articular CSI has systemic endocrine effects,[11] and patients have a 0.1% higher risk of catching flu in the following seasonal winter flu virus period following an intra-articular CSI.[7] Sytsma *et al*. considered the potential influence of CSI on contracting influenza.[12] Despite their conclusions, Little *et al*. highlighted that their results show "an absolute increase in annual infection risk of only around one in 1,000."[13] Sytsma *et al*.[12] did not specify nor follow-up on the timeline of such events, which would have been helpful when trying to draw any comparisons to the current COVID-19 coronavirus.

Studies suggest intra-articular CSI increase the risk of contracting the influenza virus, but this period of reduced immunity may only last for a matter of weeks.[5] However, no specific studies have yet been performed looking at the risk of contracting the COVID-19 virus following intra-articular CSI. While a deferral period of 2 weeks after CSI is advised before receiving the COVID-19 vaccine,[5,14] studies are needed to determine the correlation between CSI and COVID-19 risks and outcomes.

It is, therefore, evident that a localized intra-articular CSI may increase a patient's susceptibility to infection.[10,12] While some practitioners have decided to halt the administration of CSI indefinitely during the pandemic, others have decided to administer it at half dose and some at full dose. This prospective cohort study aimed to assess whether patients who received a CSI into joints of the upper and lower limbs during the COVID-19 pandemic went on to contract COVID-19 and, if they did, to assess the severity of their symptoms.

## MATERIALS AND METHODS

All adult patients who were scheduled for a CSI for musculoskeletal indications were identified. All patients received injections at private and NHS Hospitals between June 2020 and March 2021. The patients were consented formally for their respective injections and made aware specifically of the possible risk of contracting COVID-19 infection subsequent to injections. Injections were performed by a fellowship-trained consultant orthopedic surgeon and a fellowship-trained consultant radiologist.

All patients underwent awake CSI under an aseptic non-touch sterile technique in the outpatient setting, except the hip injections, which required a clean room with an image intensifier. The area for injection was prepared with a chlorhexidine preparation stick followed by a sticky isolation drape over the area for injection. Patients received either 20 or 40 mg of Depo-Medrone (Methylprednisolone) mixed with 5 mL of 0.25% Marcaine (Bupivacaine). The choice of the dose administered was according to recommendations at the time, which were for half dose initially moving to full dose.

Patients were reviewed face to face at 8 weeks and 3 months post-injection. At each visit, patients were asked if they had suffered symptoms of COVID-19 at any time post the CSI. Questions asked and the post-injection survey is outlined in [Table 1]. Patients were followed up through telephone at 6 months to ascertain if any symptoms or subsequent COVID-19 tests had been required.

If patients answered "yes" to any of the questions, they were subsequently asked if they had a test confirming

**Table 1:** Post-injection survey questions.

| |
|---|
| Have you experienced or developed any of the following symptoms since your injection? |
| - Temperature or Fever |
| - New cough |
| - New runny nose |
| - New loss of smell |
| - New loss of taste |
| - New shortness of breath or breathing difficulty |
| - New nausea and vomiting |
| - New headache |
| - Any other unusual symptoms |
| Have you had a COVID-19 test? If you did, how long after the injection? |
| If yes, what sort of test was it, Nasal/Throat swab/Polymerase chain reaction test or Blood/Antibody test? |
| If yes, what was the result? |

COVID-19. In addition, patients were asked about the severity of any symptoms suffered, whether they sought medical assistance (their GP or hospital), required hospital inpatient admission, or just isolation and management at home.

All patient demographics, ages, comorbidities, site of injection, dose of Depo-Medrone, number of injections (if applicable), the 8-week and 3-month follow-up information and any injection-related complications were recorded. Information gathered at 6-month telephone appointments was also gathered. Any subsequent intervention, such as surgery, was also recorded.

## RESULTS

A total of 224 CSI was performed during our study period. The patient demographic data and comorbidities are reported in [Table 2]. The breakdown for the location of CSI injections and Depo-Medrone dosage is outlined in [Table 3].

Seven patients underwent repeat injections within the study period, and one had bilateral injections. There were 216 individual patients. Twenty patients declined to consent to participate in the study. This resulted in a total of 196 patients (204 CSIs) included in the study.

**Table 2:** Demographic data of patients.

| Characteristic | Range (years) | Mean (years) |
|---|---|---|
| Age | 38–81 | 61 |
| Gender | | Number |
| | Male | 100 |
| | Female | 96 |
| Comorbidities | | Number |
| | Rheumatoid Arthritis | 6 |
| | Diabetes Mellitus | 12 |
| | Respiratory disorders | 6 |
| | Oncology treatment | 2 |

**Table 3:** Characteristics of injections.

| | Number |
|---|---|
| Area of injection | |
| Ankle | 15 |
| Elbow | 15 |
| Foot | 42 |
| Hand | 8 |
| Hip | 24 |
| Knee | 25 |
| Shoulder | 82 |
| Wrist | 13 |
| Steroid dosage | |
| Half (20 mg) | 90 |
| Full (40 mg) | 114 |

[Figure 1] outlines the overall flowchart for the study cohort and patient outcomes from follow-up at 8 weeks, 3 months, and 6 months.

No patients suffered symptoms nor required PCR tests within the first 8 weeks of follow-up. Twenty-one patients had negative PCR tests, required due to government contact tracing requirements, at the 3-month follow-up.

Due to their persistent musculoskeletal symptoms and discomfort, ten patients went on to have surgery between 3 and 6 months. They required PCR tests as a part of preoperative assessments, and all were negative. In addition, post-surgery, none of the patients developed symptoms by the 3-month post-operative or 6-month telephone follow-up.

A total of four patients tested positive on viral PCR: two patients between 3 and 4 month post-CSI and two patients just after 6 months. All four reported coughing symptoms alone, requiring home isolation and no further medical attention. None of them required hospitalization.

## DISCUSSION

Our study demonstrates that only 2% of patients contracted COVID-19, all of whom were after the 3-month follow-up post-CSI. These patients all reported mild symptoms and none required hospitalization.

There is a sparsity of data and information pertaining to the effect of CSI use and the risk of COVID-19 acquisition. Our study is one of the first to report our findings of patients prospectively followed to review whether there appeared to be increased risk following intervention with CSI and is one of the largest studies to date. Given the recent pandemic, this serves as important data that can be utilized for the management of such prevalent morbidities as we consider future treatments.

Our findings support previous and current national multisociety guidance, which advocates CSI use where appropriate.[5,7,15] Gan have suggested that the severity of pain and undertreatment of pain have been associated with increased infection risk and may itself impede the immune system.[16] This reinforces the importance of optimizing pain relief and the importance of the role CSI plays in the analgesic ladder.

Musculoskeletal pathology and its management are the cause of a significant health burden, with pain the primary reason for presentation in about a quarter of cases in primary care.[4,17] Oral analgesia is sometimes insufficient for controlling pain in patients and escalating interventions can involve CSI. As waiting lists rise, patients have reported debilitating pain worsening as elective procedures were canceled for long periods, putting the burden onto patients already suffering.[17]

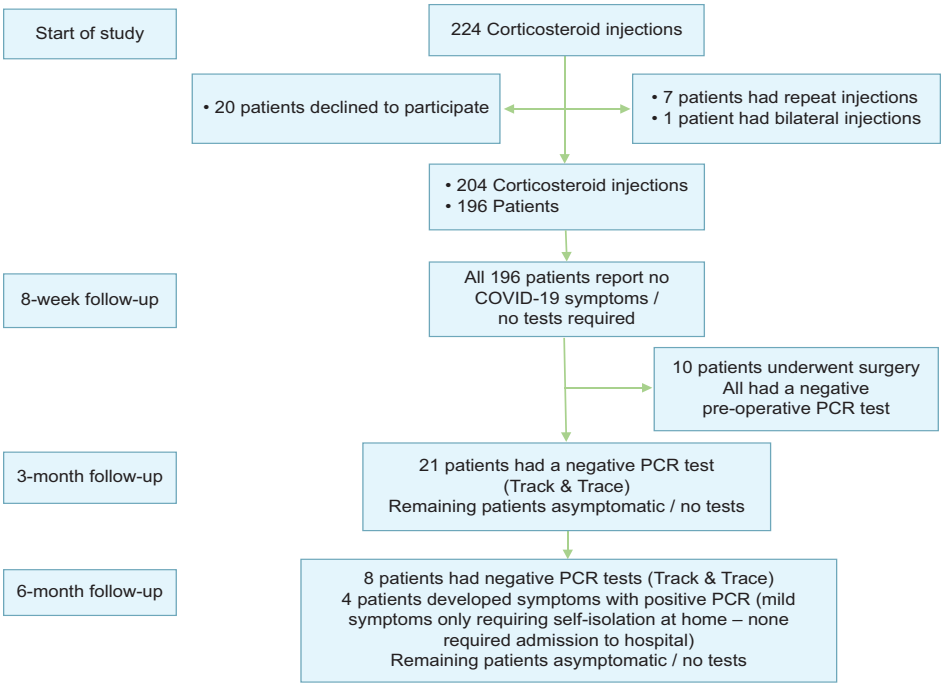


**Figure 1:** Patient cohort flow chart.

In osteoarthritis, the pain experienced has been shown to worsen the quality of life.[17] These groups of patients may well be waiting for surgical procedures such as arthroplasty and managing their debilitating symptoms, while they are awaiting their procedure can be challenging. CSI provides an important therapeutic option, especially during such a tumultuous period for the health-care sector, with long-waiting lists for elective musculoskeletal surgery[1] and sensible use of these less invasive management options may assist struggling patients during this challenging period, lessening patient pain, and improving their quality of life. CSI offers an easy and convenient method of administering effective pain relief and reducing their burden, which can lead to serious mental health problems in severe cases.[16]

We are aware that the study has limitations. The authors recognize that this is a small observational cohort study and is not sufficiently powered to provide the absolute risk of CSI definitively. We are aware of the confounders with the possibility of patient bias, reporting bias, and selection bias. A patient's home situation and their behavior in the pandemic outside of the clinical environment could make them a self-selecting cohort. No isolation precautions were taken pre- or post-procedure, but routine precautions of standard personal protective equipment in the clinic were used. An evaluation against a cohort of patients who did not receive CSI has not been analyzed and we are unable to estimate the relative risk of CSI compared to the overall population. Given that not all patients were tested, we are unable to comment on an overall incidence of COVID-19 in our patient cohort and it is crucial to note that a vast majority of COVID-19 infections are, in fact, asymptomatic. Therefore, patients within this study may have contracted COVID-19 but were asymptomatic carriers. Lavezzo *et al.* reported that 42.5% of confirmed COVID-19 infections were asymptomatic across the two nasopharyngeal swabs surveys for 85.9% and 71.5% of the population of the Italian municipality of Vo'.[18]

Our duration of follow-up was based on the clinical follow-up for CSI routinely used by the surgeon. We are unaware of the duration that CSI may reduce an individual's immunity and when a patient's immunity normalizes again. Current literature suggests this could be as little as a few weeks.[4] There remains no clear, robust evidence for the duration of suppression with CSI nor its relationship with COVID-19 infection or illness severity.[19]

Our data collection was limited to our local patients, which may introduce biases based on the demographics of the local population, including race and socioeconomic status. The authors note that our in-depth written consent process for CSI during this period, which included a lengthy discussion of the potential risk of corticosteroid-induced immunosuppression throughout the pandemic, may have led patients to take more effective precautionary measures, which may lead to a lower risk of COVID-19 infection contraction. However, our patient population was in one of the worst affected areas by COVID-19 infection, with up to 400 new cases reported daily.[20] Therefore, the surrounding prevalence would likely increase the risk posed to those patients in our study for contracting COVID-19, which therefore enhances our findings of CSI seemingly not increasing an individual's risk of susceptibility.

Future work should involve larger population-based studies and meta-analyses to understand the risk of CSI in relation to COVID-19 comprehensively. The data from our study would most likely prove helpful to future reviews.

## CONCLUSION

Our study demonstrated no obvious correlation between CSI and COVID-19 acquisition and did not identify any clear increase in risk. We would therefore endorse the use of CSI when required for patients. However, due to the small sample size, we could not conclude that musculoskeletal CSI brings no risk of contracting COVID-19 infection. However, our observation from this study would, in all probability, conclude that this appears to be minimal.

## RECOMMENDATIONS

The authors would advocate and emphasize the need for appropriate patient selection, shared decision-making with patients, a clear consenting process, and patient reassurance. We would continue to advise judicious hand hygiene and wearing personal protective equipment to help minimize other risk factors.

We suggest careful consideration of the risk-benefit to patients before administration of musculoskeletal CSI to patients who might gain the benefit of CSI effect on pain and inflammation.

## ETHICAL APPROVAL

The study was registered with the local research and audit department. This was an observational study. The local research ethics committee confirmed that no ethical approval was required.

## AUTHORS CONTRIBUTIONS

All authors contributed to the study's conception and design. Patients were recruited, and data were collected by HS, RB, and RP. Material preparation, data collection, and analysis were performed by PR, MB, and RP. The first draft of the manuscript was written by PR and all authors commented on previous versions of the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the manuscript's content and similarity index.

## USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY FOR MANUSCRIPT PREPARATION

The authors confirm that there was no use of Artificial Intelligence (AI)-Assisted Technology for assisting in the writing or editing of the manuscript and no images were manipulated using the AI.

## DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## CONFLICTS OF INTEREST

There are no conflicting relationships or activities.

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