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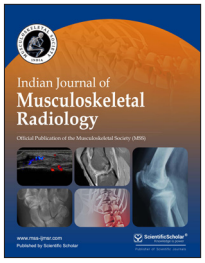

Review Article

Musculoskeletal Interventions in the era of COVID-19: Current Scenario and Review of Literature Regarding Procedures, Practices, and Precautions

Ameya Shirish Kawthalkar

Department of Radiology, Sir JJ Hospital and Grant Medical College, Sir JJ Marg, Byculla, Mumbai, Maharashtra, India.

***Corresponding author:**
Ameya Shirish Kawthalkar,
Department of Radiology,
Sir JJ Hospital and Grant
Medical College, Sir JJ Marg,
Byculla, Mumbai - 400 008,
Maharashtra, India

ameya005@gmail.com

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ABSTRACT

Given the current severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic we find ourselves in, the availability of clinically relevant and reliable information regarding any diagnostic test and therapy for clinicians and patients is of utmost importance. As SARS-CoV-2 is a new virus, there are no long-term data regarding the effect of therapeutic musculoskeletal interventions on patients infected with it. Some reports published in recent literature state that corticosteroids may exacerbate symptoms in coronavirus disease 2019 (COVID-19) while other conflicting ones show improvement in patient symptoms; however, these are based on systemic corticosteroids and not locally injected ones. A few musculoskeletal, pain management, and orthopedic societies around the world have recently published their guidelines for performing these interventions. ASRA-ESRA guidelines recommend using ultrasound guidance to perform musculoskeletal and pain interventions over "blind" non-image-guided procedures to reduce local anesthetic systemic toxicity. This article aims to review the current literature for musculoskeletal interventional practices with regard to COVID-19 and also detail the various precautions which musculoskeletal interventional radiologists can take to protect themselves and their patients from SARS-CoV-2 as per current guidelines.

Keywords: Musculoskeletal interventions, Musculoskeletal radiology, Pain interventions, Interventional radiology, Corticosteroids, COVID-19, SARS-CoV-2

INTRODUCTION

Coronaviruses are a group of single-stranded RNA viruses known to mankind since the 1930s.[1] *Corona* in Latin means a crown or wreath, and the viruses are called so because they resemble a solar corona or halo when observed under electron microscopy.[2] Various coronaviruses cause diseases ranging from rhinitis (common cold) to the severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and the newly discovered coronavirus disease 2019 (COVID-19).[3] As of writing this article, humanity finds itself in the midst of the COVID-19 pandemic which has disrupted life around the globe.[4] The coronavirus which causes the disease COVID-19 is called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[5] SARS-CoV-2 was first isolated from patients suffering from lower respiratory tract infection in Wuhan, the capital of China's Hubei Province.[6] SARS-CoV-2 is thought to be a new coronavirus not encountered previously before 2019.[3,6]

Its infectivity or R0 (basic reproduction number) is estimated to be in the range of 2.2–5.7 making it a highly infectious virus.[7] Commonly reported symptoms are fever, sore throat,

cough, myalgia, fatigue, anosmia, malaise, nausea, vomiting, and diarrhea.[8] Complications of COVID-19, seen in critically ill patients, include acute respiratory distress syndrome, myocardial ischemia, myocarditis, acute renal injury, secondary infection, cytokine storm syndrome, pulmonary embolism, and hemorrhagic encephalitis among others.[9] At present, no obvious musculoskeletal symptoms (other than myalgia and arthralgia) or complications due to COVID-19 have been reported in published literature.[8] Median incubation period of the disease is 5.1 days.[10] Morbidity and mortality are highest in elderly population.[11] Along with this, recent studies demonstrate a large proportion of SARS-CoV-2 carriers which are asymptomatic with the percentage of asymptomatic carriers in a given population estimated to range between 30 and 56%.[12]

Being a new virus, there are no long-term studies available regarding the effects of musculoskeletal interventions on patients with COVID-19. Some reports published recently state that corticosteroids may exacerbate symptoms in COVID-19 while other conflicting ones show improvement in patient symptoms; however, these are based on systemic corticosteroids and not locally injected ones.[13] A few musculoskeletal and pain intervention societies worldwide have recently published guidelines for performing musculoskeletal interventions with regard to COVID-19. This article aims to review current literature regarding musculoskeletal interventional practices with regard to COVID-19, both in COVID-19 patients and in the non-COVID-19 population after the advent of the COVID-19 pandemic. It also details the precautions which musculoskeletal interventional radiologists can take to protect themselves and their patients from COVID-19 according to current guidelines.

MATERIAL AND METHODS

A literature search was conducted in PubMed and Google Scholar with the keywords musculoskeletal interventions, corticosteroids, and NSAIDs each paired with the keywords COVID-19 and SARS-CoV-2. A total of 2586 search results were obtained. Out of these, review articles published in PubMed indexed journals and relevant for musculoskeletal interventions, corticosteroids, and NSAIDS in relation to the COVID-19 pandemic were considered for review (a total of 27 such articles were obtained). The international guidelines from various musculoskeletal and pain societies obtained from Google search using the keywords "musculoskeletal interventions, corticosteroid injections COVID-19" were included in the review (a total of six guidelines). International guidelines for musculoskeletal interventions were sourced from the individual websites of the societies publishing them.

GENERAL CONSIDERATIONS IN PATIENTS WITH MUSCULOSKELETAL DISORDERS AND CHRONIC PAIN

Apart from amateur and professional sportspersons, a large majority of the patient population undergoing image-guided therapeutic musculoskeletal interventions consists of middle-aged and elderly people with chronic pain. A few of these are the so-called "weekend warriors" who injure themselves during sudden unaccustomed exercise.[14]

Some are young patients requiring image-guided ablation for bone and soft-tissue neoplasms such as osteoid osteoma, chondroblastoma, and fibromatosis.[15] Patients with osteoporotic or malignant neoplastic fractures of vertebrae are candidates for vertebroplasty and kyphoplasty.[16] Certain patients with chronic nerve pain undergo image-guided nerve blocks. These can be pain due to impingements, post-traumatic neuromas, or infiltration by neoplasms.[17] Diagnostic musculoskeletal interventions such as image-guided biopsies, fine-needle aspiration cytology (FNAC), and aspirations may be required in patients with bone and soft-tissue neoplasms and infections (such as tuberculosis).[18] All these patients are at risk of having multiple comorbidities and some may have potential immune suppression.

Considerations for musculoskeletal interventions in the COVID-19 era include:

a. Determining the need and timing of a musculoskeletal intervention for a patient
b. Taking adequate precautions to ensure infection prevention for the patient, doctors, and all staffs involved
c. Understanding the safety of the injectable drugs and peri-procedural medications used in musculoskeletal interventions in relation to COVID-19 based on available and evolving evidence in literature and implementing the same in practice

COVID-19, CORTICOSTEROIDS, AND THE IMMUNE SYSTEM

Effective innate immune response of the body against viruses depends predominantly on the interferon (IFN) type I pathway. SARS-CoV and MERS-CoV which are the two coronaviruses sharing genetic similarities with SARS-CoV-2 are both known to suppress the type I IFN pathway. It is speculated that SARS-CoV-2 employs similar strategies to suppress the innate immune system, especially by dampening the type I IFN response, but other additional mechanisms of action of the virus may be uncovered with future research.[19]

Like SARS-CoV, SARS-CoV-2 is postulated to act through the angiotensin-converting enzyme-2 (ACE2) receptor. ACE2 is mainly expressed in type 2 alveolar cells in the lungs

and also expressed in small intestine, kidneys, brain, and other organs.[20]

Systemic corticosteroids have been shown to dramatically inhibit the IFN type I pathway of innate immunity.[21] In addition, corticosteroids alter the function of virtually all immune cells.[22] However, these findings are based on systemic or inhaled corticosteroids. Recently, there have been a number of reports of intra-articular injection of corticosteroids, leading to transient suppression of the hypothalamus-pituitary-adrenal (HPA) axis.[23] Many viral infections activate the HPA axis through the release of cytokines, after which the axis acts to strengthen the immune response against the virus. Suppression of the HPA axis has shown to increase mortality related to viral infections.[24] A recent study also showed increased risk of influenza in patients receiving intra-articular corticosteroid injections.[25]

COVID-19 AND NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

Oral nonsteroidal anti-inflammatory drugs (NSAIDs) are routinely prescribed in patients with musculoskeletal pains, including following musculoskeletal interventions. A small anecdotal report in France of only four patients reported worsening of symptoms in COVID-19 after the administration of ibuprofen.[26] However, a rapid systematic review performed by the World Health Organization (WHO) of 73 studies on this subject revealed no evidence of severe adverse events, effect on long-term survival or quality of life in patients with COVID-19 as a result of the use of NSAIDs.[27]

REVIEW OF CURRENT INTERNATIONAL GUIDELINES FOR MUSCULOSKELETAL AND PAIN INTERVENTIONS

A. Diagnostic musculoskeletal interventions:
   These include ultrasound and CT-guided biopsies, FNACs, and aspirations. At present, most of the guidelines do not deal expressly with diagnostic interventions in the setting of the COVID-19 pandemic; however, the Australasian Musculoskeletal Imaging Group (AMSIG) advises to continue performing musculoskeletal interventions with informed consent.[28] Optimum infection prevention protocols should be followed for these interventions.
B. Therapeutic musculoskeletal interventions:
   1. Image-guided musculoskeletal injections:
      These include but are not limited to corticosteroids, platelet-rich plasma (PRP), hyaluronic acid, local anesthetics, dextrose, sclerosants, etc. The current guidelines all deal with corticosteroids in relation to COVID-19, and one guideline also covers local anesthetics. A summary of these recommendations made by various international societies for musculoskeletal and pain interventions during the COVID-19 pandemic which are summarized in Table 1.[28-33] Interventions classified as urgent and semi-urgent by ASRA and ESRA are enumerated in Table 2.[33] The ASRA-ESRA guidelines on regional anesthesia also recommend ultrasound guidance over blind procedure to reduce systemic toxicity of local anesthetics.[34]
   2. Other image-guided therapeutic musculoskeletal interventions:
      These include thermal ablation procedures, vertebroplasty, kyphoplasty, and musculoskeletal embolizations. As of writing, a literature search did not reveal any published material on status of these interventions specifically during the COVID-19 pandemic, other than the AMSIG recommendations to continue musculoskeletal interventions with informed consent.[28]

REVIEW OF CURRENT RECOMMENDED SAFE PRACTICES FOR INTERVENTIONAL RADIOLOGISTS

Once community transmission of SARS-CoV-2 in a region or country is significant, precautions must be taken while performing musculoskeletal interventions reckoning that every patient could be COVID-19 positive. Local and national guidelines regarding conduct of these procedures should be followed. Standardized operating procedures should be made within the department or radiology practice for performing musculoskeletal interventions in patients with COVID-19 and those without COVID-19 in accordance with regional guidelines and recommendations. Risk versus benefit ratio should be assessed for each patient for the intervention, after discussion with the referring physician.

Patient movement should be limited within the department/radiology clinic. Patients should be encouraged to wear surgical masks to minimize droplet infection spread. During the procedure, all staffs involved with confirmed patients of COVID-19 or patients in whom COVID-19 has not been excluded must follow a high-standard infection protection protocol, including wearing a complete personal protective equipment (PPE) kit (recommended). In dealing with patients, in whom COVID-19 has not been confirmed, at the minimum wearing of an N95 mask, gown, gloves, and a face shield should be followed. If ultrasound-, CT-, and fluoroscopy-guided interventions are performed, sterilization of the machine and probe should be performed as per manufacturer specifications. Local and hospital guidelines must be followed for medical waste disposal. Replacement of all medical sheets is recommended after each procedure.[35]

Table 1: Summary of current international guidelines for musculoskeletal and pain interventions.

Name	Date published	Drug/procedure	Recommendation
Faculty of Pain Medicine, Royal College of Anaesthetists[29]	March 17, 2020	Corticosteroids	Impact of injected corticosteroids on COVID-19 unknown. Evaluate risk versus benefits in each individual case.
British Society of Skeletal Radiology (BSSR)[30]	March 19, 2020	Corticosteroids	Avoid musculoskeletal or perineural corticosteroid injections wherever possible during COVID-19 pandemic, especially in high-risk patients. Consider other non-corticosteroid interventions. Some situations may still warrant use of corticosteroid injections.
American Academy of Physical Medicine and Rehabilitation (AAPMR)[31]	March 20, 2020	Corticosteroids	Although no evidence to suggest corticosteroid injections result in a substantial increase in risk of being infected with COVID-19, there is evidence noting a reduced immune response with corticosteroid administration. Exercise caution with the use of corticosteroids, particularly in higher risk patients who may be immunocompromised.
British Society of Rheumatology (BSR), Chartered Society of Physiotherapy (CSP), British Association of Spine Surgeons (BASS), and British Orthopedic Association (BOA)[32]	March 23, 2020	Corticosteroids	Corticosteroid injections to be performed only in significant musculoskeletal disease activity and if no other alternative available. Consider corticosteroids in inflamed joints with synovitis, effusion. In non-inflammatory musculoskeletal disorders consider corticosteroids in those with high level of pain, disability, and those failing first-line therapy. In general, avoid corticosteroid injections for spinal pain. Can be considered for severe radicular pain.
Australasian Musculoskeletal Imaging Group (AMSIG)[28]	March 25, 2020	General features	Continue performing musculoskeletal interventions during COVID-19 pandemic with informed consent. Clarifies that the BSSR recommendations do not imply complete cessation of corticosteroids.
American Society of Regional Anesthesia and Pain Medicine (ASRA) and European Society of Regional Anesthesia and Pain Therapy (ESRA)[33]	March 27, 2020	General features	Divides interventions into urgent and semi-urgent. Perform only urgent interventions in COVID-19 patients and high-risk patients. Perform urgent and semi-urgent interventions in COVID-19 negative or low-risk patients.
		NSAIDs	Continue use. Educate patients to promptly report new fever or new myalgia
		Corticosteroids	Consider decreasing dose in high-risk populations. Look for alternatives to corticosteroids. Dexamethasone and betamethasone may cause less immune suppression.

Table 2: ASRA and ESRA classification of pain interventions for COVID-19 pandemic.

Urgent	Semi-urgent
a) Intrathecal pump refill b) Neurostimulator infection and malfunction.	a) Intractable cancer pain b) Acute herpes zoster or subacute, intractable post-herpetic neuralgia c) Acute herniated disc and/or worsening lumbar radiculopathy d) Intractable trigeminal neuralgia e) Early complex regional pain syndrome f) Acute cluster headaches and other intractable headache conditions g) Other intractable medically resistant pain syndromes (should be reviewed on a case-by-case basis)

As per the Society of Interventional Radiology guidelines, musculoskeletal interventions are not considered aerosol-generating procedures.[36] However, if endotracheal intubation is performed for general anesthesia for performing a musculoskeletal intervention (such as thermal ablation), the intubation is considered an aerosol-generating procedure, which is known to be associated with releasing a high load of virions from patients with COVID-19.[37]

CONCLUSION

Image-guided musculoskeletal interventions are a varied group of procedures with a diverse spectrum and patient population. A large number of these patients may have systemic comorbidities and high-risk factors such as advanced age, disseminated solid or hematological

neoplasms, disseminated infections, diabetes mellitus, and cardiovascular disease, putting them at increased risk for severe presentation of COVID-19. It is necessary to triage patients needing musculoskeletal and pain interventions, and the interventions should be performed assessing the benefits versus risks for the patient, after discussion with the referring physician. These guidelines can be used as a tool by musculoskeletal interventional radiologists to take a decision on performing musculoskeletal interventions, especially corticosteroid injections, in the current COVID-19 pandemic scenario. Further, evidence-based guidelines looking into corticosteroid alternatives such as PRP and hyaluronic acid injections in times such as the COVID-19 pandemic would be welcome. As per the recent WHO review, there is no evidence of adverse effects in COVID-19 patients associated with NSAID use.

In this "new normal" of COVID-19, especially in regions with significant community transmission, for the safety of musculoskeletal interventional radiologists and their patients, it is imperative to consider every patient walking into the clinic for a musculoskeletal intervention as being positive for COVID-19 and take adequate precautions.

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Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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