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Did COVID-19 related delays in surgical management lead to patient morbidity in the orthopaedic oncological population?

A RETROSPECTIVE OBSERVATIONAL SINGLE CENTRE STUDY

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Aims

The aim of this study was to assess orthopaedic oncologic patient morbidity resulting from COVID-19 related institutional delays and surgical shutdowns during the first wave of the pandemic in New York, USA.

Methods

A single-centre retrospective observational study was conducted of all orthopaedic oncologic patients undergoing surgical evaluation from March to June 2020. Patients were prioritized as level 0-IV, 0 being elective and IV being emergent. Only priority levels 0 to III were included. Delay duration was measured in days and resulting morbidities were categorized into seven groups: prolonged pain/disability; unplanned preoperative radiation and/or chemotherapy; local tumour progression; increased systemic disease; missed opportunity for surgery due to progression of disease/lost to follow up; delay in diagnosis; and no morbidity.

Results

Overall, 25 patients met inclusion criteria. There were eight benign tumours, seven metastatic, seven primary sarcomas, one multiple myeloma, and two patients without a biopsy proven diagnosis. There was no priority level 0, two priority level I, six priority level II, and 17 priority level III cases. The mean duration of delay for priority level I was 114 days (84 to 143), priority level II was 88 days (63 to 133), and priority level III was 77 days (35 to 269). Prolonged pain/disability and delay in diagnosis, affecting 52% and 40%, respectively, represented the two most frequent morbidities. Local tumour progression and increased systemic disease affected 32% and 24% respectively. No patients tested positive for COVID-19.

Conclusion

COVID-19 related delays in surgical management led to major morbidity in this studied orthopaedic oncologic patient population. By understanding these morbidities through clearer hindsight, a thoughtful approach can be developed to balance the risk of COVID-19 exposure versus delay in treatment, ensuring optimal care for orthopedic oncologic patients as the pandemic continues with intermittent calls for halting surgery.

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Introduction

The COVID-19 pandemic is an unprecedented and ongoing world event, caused by SARS-CoV-2. What began as a zoonotic infection in Wuhan, China, rapidly spread

throughout the world, with the first reported case in the USA on 20 January 2020.¹ New York City was one of the hardest hit areas during the first peak of the virus and all hospitals had to radically change their

operating procedures in order to handle the surge of infected patients. By 11 March 2020, one of the tertiary institutions in our health system had their first four hospitalized in-house patients. Three days later, the entire orthopaedic floor had been converted to a COVID-19-only unit and on 15 March 2020, all elective surgeries were cancelled for the foreseeable future. To minimize the spread of the virus, all surgical procedures were triaged and assigned a priority level based on the relative urgency of the planned surgery, in accordance with the American College of Surgeons (ACS).²

The priority levels ranged from 0 to IV, with 0 being used for procedures that had no urgency - such as elective cosmetic cases where the timing of the procedure has no impact on the clinical outcome - and IV for emergency procedures, with immediate danger for life and limb. Priority III included all patients where any delay beyond four weeks would lead to significant risk of patient harm, increased surgical complexity, or hospitalization. Priority II included all patients where any delay beyond three months would lead to significant patient harm. Priority I included patients where a delay beyond six months poses minor or no risks of patient harm. A similar acuity classification system would later be described by Navarro et al³ in a manuscript on orthopaedic systems response. As most orthopaedic oncology cases were assigned as I, II, or III, combined with the fact that case scheduling was significantly limited, the majority of orthopaedic oncological procedures were delayed. The effect that these delays had on the treatment of patients with orthopaedic oncological disease, and the resultant patient outcomes, is unknown.

We defined “delay in surgical intervention” as time from the date of expected intervention to the date of actual intervention. In normal non-pandemic times, there are bi- or tri-weekly dedicated operating room availabilities during which procedures are routinely scheduled. Additionally, cases can be scheduled for any day of the week as necessary as the operating room and surgeon’s schedule allows. Surgery therefore typically occurs either the same day it is scheduled or within a week. While delays in surgery due to variables such as medical clearance, equipment processing, or patient compliance do happen, they tend to be minimal, and therefore any reported delay represents time in addition to the normal expectation.

Medical centres throughout the world have sought to understand how COVID-19 has affected the practice of medicine. Most of this research is focused on outcomes of patients infected with COVID-19. There is little research, however, regarding noninfected patients whose delay in care may have led to grave indirect sequelae. There have been studies in general cancer diagnosis and care, including more common cancers, however published work related to orthopaedic oncology is scarce.⁴ The

goal of the present study is to investigate variations in care due to delay in treatment and to analyze the resultant outcomes, with a hypothesis that COVID-19 related delays in orthopaedic oncological care led to major patient morbidity. The hope is that this knowledge will then allow for a better understanding of how to effectively manage and prioritize such patients in the event of a future pandemic.

Methods

This single-centre retrospective observational study, approved by our institutional review board, included all oncological patients undergoing surgical evaluation by the division of musculoskeletal oncology, composed of three musculoskeletal oncologists (SK, SK, and HJG), during the COVID-19 pandemic from the period of March to June 2020 in New York, USA. Informed consent was not required for this study. Inclusion criteria were as follows: patients of all ages with oncological diagnoses listed as benign, metastatic, primary limb sarcoma, multiple myeloma, or biopsy unproven disease, who experienced a delay in management due to health system-wide COVID-19 restrictions. Only priority levels 0 to III were included. All priority level IV patients were excluded as these patients qualified as emergent and therefore did not experience any delay in management. The total duration of delay was measured in days from the estimated date of planned intervention or start of the surgical shutdown to the actual date of intervention. Delay-related morbidities and outcomes were recorded and categorized into the following seven groups: 1) prolonged pain/disability, 2) unplanned preoperative radiation and/or chemotherapy, 3) local tumour progression, 4) increased systemic disease, 5) missed opportunity for surgery due to progression of disease or lost to follow-up, 6) delay in diagnosis, and 7) no morbidity.

Statistical analysis. Statistical analyses included assessing the mean duration of delay, stratified by priority level, with a two-tailed independent-samples *t*-test comparing all priority groups, in addition to a single factor analysis of variance (ANOVA), performed using Microsoft Excel (USA). Significance was set at $p < 0.05$.

Results

A total of 25 patients met the inclusion criteria in this observational study (Table I). The mean age was 45 years (15 to 86) with 14 males and 11 females. There were eight benign tumours, seven metastatic, seven primary sarcomas, one multiple myeloma, and two patients without a confirmed biopsy proven diagnosis. Priority level was assigned according to our institution’s protocol as 0 to IV with increasing urgency represented by a higher level (0 being the least urgent and IV being the most emergent). There were no priority level 0 cases, two priority level I, six priority level II, and 17 priority level III,

Table 1. Summary of results. Priority level was assigned according to the following institution protocols - Level 0: non-urgent, timing of the procedure does not affect clinical outcome; Level I: delay beyond six months poses minor or no risks of patient harm; Level II: delay beyond three months risks patient harm; Level III: delay beyond four weeks increases risk of patient harm, increased surgical complexity, or hospitalization; Level IV: delay would cause immediate severe harm or death.

Variable	Patients, n
Patients included	25
Mean age, yrs (range)	45 (15 to 86)
Sex, n	
Male	14
Female	11
Tumour type, n (%)	
Benign	8 (32)
Metastatic	7 (28)
Sarcoma	7 (28)
Multiple myeloma	1 (4)
Unknown (pending confirmation biopsy)	2 (8)
Priority level, n (%)	
0	0 (0)
I	2 (8)
II	6 (24)
III	17 (68)
IV	Excluded
Mean duration of delay, days (range)	84 (38 to 269)
Mean delay by priority, days (range)	
0	N/A
I	114 (84 to 143)
II	88 (63 to 133)
III	62 (35 to 120)
IV	Excluded
Morbidity caused by delay, n (%)	
Prolonged pain/disability	13 (52)
Unplanned radiation therapy/chemotherapy	3 (12)
Local tumour progression	8 (32)
Increased systemic disease	6 (24)
Missed opportunity for surgery due to progression of systemic disease or lost to follow-up	3 (12)
Delay in diagnosis	10 (40)
None	5 (20)
Benefit of delay (avoided surgery due to resolution of symptoms)	1
COVID-19 status at time of surgery	
Positive	0
Negative (never having tested positive)	18
Unknown	7

N/A, not available.

with all level IV cases excluded. Overall, the mean duration of delay was 84 days (range, 34 to 269). Stratified by priority level, the mean duration of delay for priority level I was 114 days (range, 84 to 143 days), priority level II was 88 days (range, 63 to 133 days), and priority level III was 77 days (35 to 269 days). Two-tailed independent-samples *t*-test and ANOVA testing revealed no significant difference in duration of delay among all priority levels with $p > 0.05$. None of the patients included in the study

were known to be COVID-19-positive, with 18 patients having a confirmed negative COVID-19 PCR test and seven patients having an unknown COVID-19 status. There were no mortalities.

The delay in treatment due to the COVID-19 pandemic resulted in several categories of morbidities, listed in Figure 1. Three patients experienced unplanned additional radiation and/or chemotherapy due to the delay. An illustrative example (Figure 2) shows a 76-year-old female whose 38-day delay necessitated a proximal humerus arthroplasty for metastatic lung carcinoma, with the surgery becoming more challenging due to rapid progression, despite the additional radiation given during the COVID-19-imposed delay. The other two patients, both with diagnoses of osteogenic sarcoma, received an additional cycle of chemotherapy.

Eight patients experienced local tumour progression while four patients suffered from increased systemic tumour burden due to the COVID-19 related delay in treatment. These patients included a 64-year-old male with a forearm undifferentiated pleomorphic sarcoma, assigned as a level III priority, who experienced a delay of 110 days, and had to undergo a more complicated and wider resection given the significant interval local tumour progression (Figure 3). Another included an 86-year-old female with metastatic lung carcinoma to the proximal femur who was assigned as a level III priority, experienced a delay of 49 days, and had a more complex resection and reconstruction as a result. One of the most serious sequelae of the delay was seen in a 31-year-old male with a subungual high-grade melanoma of the left long finger who may have had systemic spread due to a delay in surgery by 43 days. This patient had a negative positron emission tomography (PET) scan preoperatively and was assigned a level III priority, however during restaging for the delayed surgery this patient was found to have a positive axillary lymph node, showing increased systemic tumour burden during this time interval (Figure 4).

Three patients experienced a missed opportunity for surgery due to progression of systemic disease, or were lost to follow-up as a result of their COVID-19 related delay. One of these patients, a 71-year-old male, had metastatic bladder cancer to the left acetabulum and was planning to undergo a left total hip arthroplasty. The patient was assigned a priority level of III, but while waiting for a surgical date, the patient experienced an overall decompensation in medical status and was never able to be cleared for surgery. Ten patients experienced a delay in diagnosis due to a delay in biopsy as a result of either scheduling restrictions or due to patients' fear about follow-up and possible COVID-19 infection.

There were 13 patients who experienced prolonged pain and/or disability due to a delay in treatment, which represented the most frequent morbidity in this cohort, affecting 52% of patients. An example of such a patient

Morbidity due to COVID-19 Related Delays

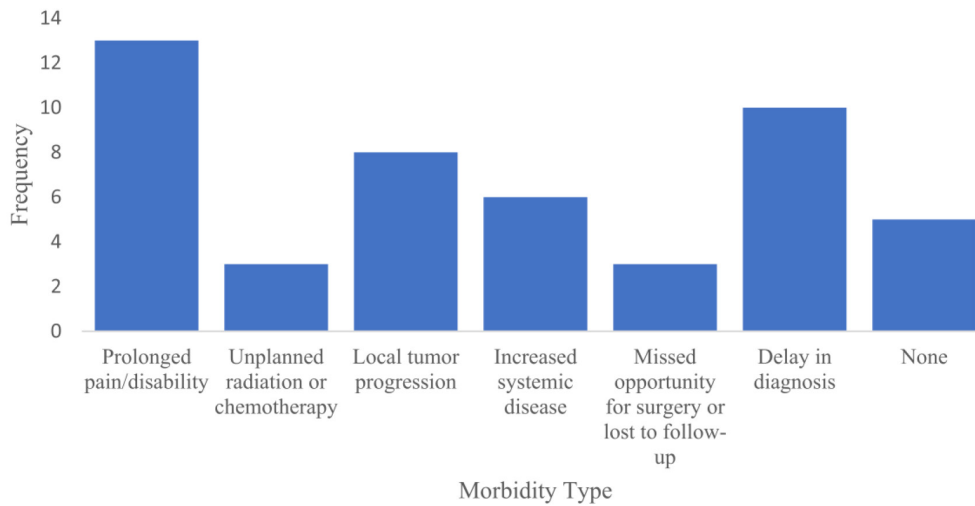


Fig. 1

Morbidity due to COVID-19 related delays. The most common morbidity was prolonged pain/disability (52%). The second most common morbidity was a delay in diagnosis (40%).



Fig. 2

76-year-old female with poorly differentiated metastatic lung carcinoma to bone, prioritized as level III. Anteroposterior (AP), external rotation, and internal rotation radiographs of the left humerus, a) and b) 11 February 2020 and c) and d) 24 April 2020. e) Postoperative AP view, 2 May 2020. Extensive progressive interval osseous destruction with extraosseous soft tissue mass involving the left proximal humerus to mid-shaft diaphysis with associated pathological fracture. Due to COVID-19 related delays, this patient experienced prolonged pain and disability, unplanned radiation, and local tumour progression resulting in markedly increased surgical complexity.

was a 43-year-old male who was scheduled to undergo a left knee open synovectomy for tenosynovial giant cell tumour. The patient was assigned a priority level II and therefore had to endure persistent knee pain and difficulty with ambulation for 91 days due to delay in management.

Five patients experienced no associated morbidity, while one patient had complete resolution of her local

disease after radiation, thus avoiding surgery altogether. This patient, a 57-year-old female, had a diagnosis of multiple myeloma with a large lesion in the right proximal humerus causing significant pain and an impending pathological fracture. The patient was planned to undergo a curettage with open reduction and internal fixation of the lesion, as a priority level III. However, while awaiting a surgical date, she received palliative radiation

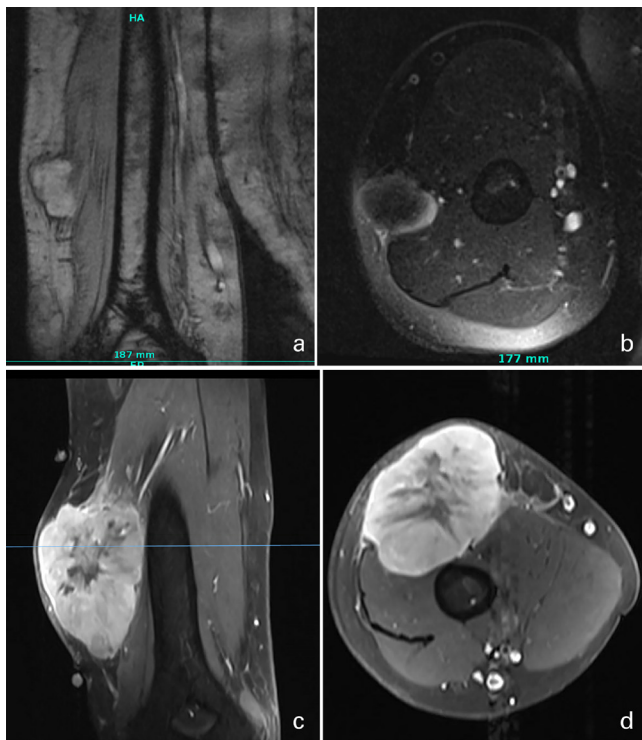


Fig. 3

64-year-old male with undifferentiated pleomorphic sarcoma of the right arm, prioritized as level III. a) Coronal and b) axial MRI of the right humerus demonstrating a 2.1 × 2.2 × 3.3 cm well-defined lateral subcutaneous lesion at the level of the distal humeral diaphysis, 25 March 2020. c) Coronal and d) axial MRI of the right humerus demonstrating significant interval enlargement of an enhancing lobulated mass of the right arm, 7.8 × 4.8 × 4.6 cm, 8 July 2020. Due to COVID-19 related delays, this patient experienced a delay in diagnosis and marked local tumour progression, leading to a substantial increase in surgical complexity with a resulting wider resection.

which ultimately led to a complete cessation of pain with interval radiological resolution and healing around the initial lesion, obviating a need for surgical intervention.

Discussion

The acute effects of COVID-19 on patients are now well known. Per the Centers for Disease Control and Prevention (CDC), symptoms generally appear two to 14 days after exposure to the virus and may include fevers/chills, cough, shortness of breath, fatigue, muscle/body aches, headaches, loss of smell/taste, sore throat, congestion, nausea/vomiting, and diarrhea.⁵ Medical sequelae can include acute/chronic multisystem organ damage leading to interstitial pulmonary fibrosis, inflammatory myocarditis, renal failure, stroke, encephalomyelitis, venous thromboembolism (VTE), and death.⁶

The COVID-19 pandemic has had a major impact in the field of orthopaedics with reported increased mortality rates throughout the world. A British multicentre retrospective cohort study comparing 340 COVID-19-negative patients to 82 COVID-19-positive patients undergoing hip fracture surgery revealed a three-fold increase in

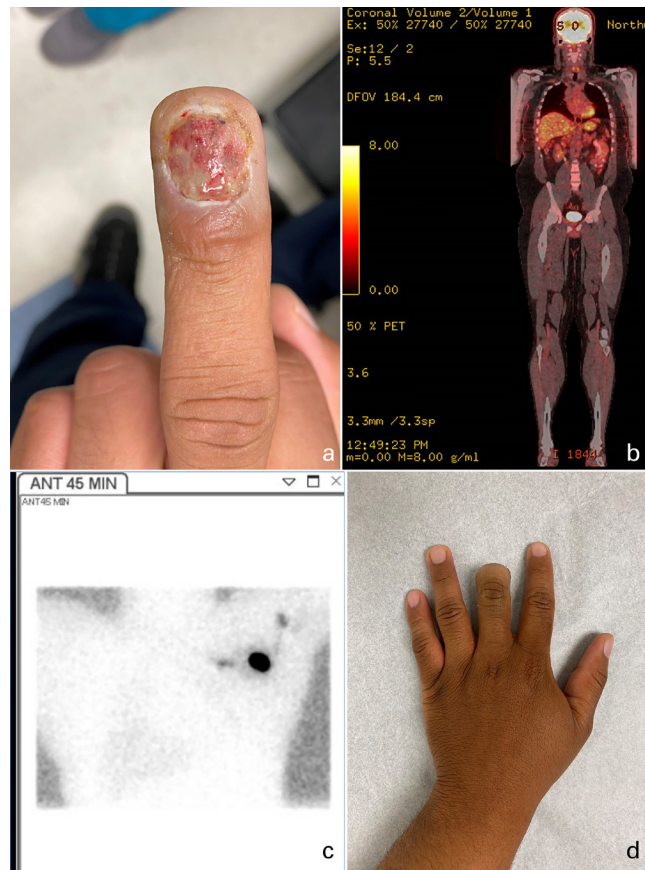


Fig. 4

31-year-old male with high-grade malignant melanoma of the left long finger, prioritized as level III. a) Gross image, 16 March 2020. b) Preoperative coronal positron emission tomography scan, negative for systemic pathological fluorodeoxyglucose uptake, 25 March 2020. c) Lymphoscintigraphy on the day of surgery (20 May 2020), demonstrating left axillary and pectoral nodal accumulation of radiopharmaceutical material. d) Postoperative gross image. Final pathology of the axillary lymph node was positive for malignant melanoma. Due to COVID-19 related delays, this patient may have experienced increased systemic tumour progression.

mortality rate, in addition to increased length of stay and increased risk of perioperative complications in COVID-19-positive patients.⁷ A multicentre study in Scotland demonstrated similar findings, with a nearly two-fold increased mortality rate in COVID-19-positive patients undergoing orthopaedic surgery as compared to noninfected controls.⁸ These findings were echoed in New York, where a prospectively collected data analysis demonstrated a 35% risk of mortality in COVID-19-positive patients, as compared to 7.1% for COVID-19-suspected and 0.9% for COVID-19-negative patients undergoing hip fracture surgery.⁹

With regards to oncological patients, the effects of COVID-19 infection are even more dramatic due to their immunosuppressed status. In addition, cancer patients were shown to react differently to COVID-19 therapies such as high-dose corticosteroids, hydroxychloroquine, and Remdesivir with a poorer tolerance threshold of

residual side effects. A meta-analysis by Giannakoulis et al,¹⁰ involving 1,776 cancer patients infected with COVID-19 from Asia, Europe, and the USA, revealed a significantly higher all-cause mortality and need for intensive care unit admission as compared to controls without cancer, with a relative risk of 1.66. According to recently released data from the COVID-19 & Cancer Consortium (CCC19) on 2,186 adults with cancer and COVID-19 in the USA, cancer patients infected with COVID-19 had a three times increased risk of death.¹¹ These compelling studies emphasize the importance of doing everything possible to prevent an oncological patient from contracting COVID-19.

Nevertheless, the literature is limited regarding how COVID-19 has affected infected orthopaedic oncological patients and is completely absent with regards to the care of noninfected orthopaedic oncological patients. Stevenson et al¹² showed that of 100 patients with primary malignant bone or soft tissue tumours undergoing treatment during the pandemic, the 30-day mortality rate was 1% overall and 20% in patients who contracted COVID-19. Within their study cohort, 5% of the patients were diagnosed with COVID-19. They concluded that with appropriate perioperative measures to prevent viral transmission, urgent orthopaedic oncology procedures should continue during a pandemic without excessive risk to the patient. Şahbat et al,¹³ in their review of managing orthopaedic oncology patients during the pandemic, concluded that instituting a strict protocol limiting patient exposure to any potentially infected staff was essential to minimizing spread of the virus. They limited entrances and exits from and minimized the number of people in the operating room, did not allow visitors in the hospital, only allowed one visit to each patient by the operating physician a day, and limited entrances to a patient's hospital room. Three patients were suspected to have COVID-19 prior to surgery. None of the remaining 113 patients had perioperative nosocomial transmission. Olshinka et al¹⁴ also investigated how best to triage orthopaedic oncological patients to limit patient exposure to possible carriers of COVID-19. They used a telephone referral and pre-clinic evaluation system to ensure that only patients with confirmed or suspected high-grade malignancies would be seen in the clinic. Patients were still discussed at multidisciplinary meetings, but these were virtual. This approach allowed them to limit exposures while still maintaining a high degree of orthopaedic oncology care.¹⁴ A similar approach was used in our institution, which has been beneficial in continuing to triage patients after the initial wave passed.

Although there is a wealth of knowledge being continuously reported on the direct effects of COVID-19, little has been described concerning its indirect effects on oncological patients due to delay in management. We have identified seven different adverse outcomes due to

these delays. All the patients in this cohort had a delay in care due to system-mandated surgical shutdowns and risk stratifications, several of whom experienced dramatic progression of disease with management-altering implications. The most profound morbidities observed were local and systemic progression of disease due to this delay in care. These complications were a direct result of severely limited resources, staffing, and available patient beds during a time of acute crisis. In addition, there were attempts at protecting these patients from unnecessary COVID-19 exposure, which could have led to potentially still graver outcomes. Thankfully, none of the patients in this study have tested positive for COVID-19 and therefore did not suffer from any COVID-19 related sequelae. In that regard, the risk stratification system implemented was a success as it kept these patients safe from viral transmission. While the number of patients included in this study is low, we do believe it is reflective of the general orthopaedic oncological patient population, and likely underestimates the depth of patient morbidity sustained as a result of COVID-19 related delays in care. Future studies may focus on this particular patient cohort on a larger scale to assess the long-term impact of these delays with regards to patient outcome and survival.

Moving forward, we believe priority level III patients, being the most vulnerable group for developing early delay-related complications, should be more carefully scrutinized with all efforts to proceed with surgery, while maintaining the strictest protocols of safety and protection from COVID-19. Extra care should be given to these patients including isolated rooms, use of personal protective equipment, and limited contact with providers and staff except when necessary. Additionally, these patients should be actively followed and reassessed frequently to determine if their priority level should be increased based on clinical and imaging findings. In an ideal world, all surgeries would proceed as planned, with all patients and staff members adequately protected from the disease. In reality however, restrictions need to be placed to prevent virus transmission while preventing unnecessary and possibly disease-altering delays. Being aware of the potential delay-related morbidities, as described in this cohort, can aid the orthopaedic oncologist in properly balancing the risk of COVID-19 against the risk of delayed intervention.

We are unfortunately still in the infancy of this devastating pandemic, with little known regarding the long-term effects of COVID-19 and even less regarding the indirect impacts of COVID-19 on healthcare systems and, in particular, the more fragile oncological patient population. Promising new data regarding vaccines are being released, with the first vaccination in the USA occurring on 14 December 2020 at our institution, Northwell Health.¹⁵ As more data is processed, we will have a better understanding of this unusual virus, its implications, and

the ideal method of prioritizing and managing orthopaedic oncology patients during times of crisis such as the COVID-19 pandemic.

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- H. J. Goodman: Conceptualized and designed the study, Acquired, analyzed, and interpreted the data, Drafted, revised, and approved the article.
- S. Kenan: Conceptualized and designed the study, Acquired, analyzed, and interpreted the data, Drafted, revised, and approved the article.
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