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RESEARCH ARTICLE

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Mortality of high-risk orthopaedic oncology patients during the COVID-19 pandemic: A prospective cohort study

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Abstract

Background and Objectives: Should the threshold for orthopaedic oncology surgery during the coronavirus disease-2019 (COVID-19) pandemic be higher, particularly in men aged 70 years and older? This study reports the incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during, respiratory complications and 30-day mortality during the COVID-19 pandemic.

Methods: This prospective observational cohort study included 100 consecutive patients. The primary outcome measure was 14-day symptoms and/or SARS-CoV-2 test. The secondary outcome was 30-day postoperative mortality.

Results: A total of 100 patients comprising 35 females and 65 males, with a mean age of 52.4 years (range, 16-94 years) included 16 males aged greater than 70 years. The 51% of patients were tested during their admission for SARS-CoV-2; 5% were diagnosed/developed symptoms of SARS-CoV-2 during and until 14 days post-discharge; four were male and one female, mean age 41.2 years (range, 17-75 years), all had primary malignant bone or soft-tissue tumours, four of five had received immunosuppressive therapy pre-operatively. The 30-day mortality was 1% overall and 20% in those with SARS-CoV-2. The pulmonary complication rate was 3% overall.

Conclusions: With appropriate peri-operative measures to prevent viral transmission, major surgery for urgent orthopaedic oncology patients can continue during the COVID-19 pandemic. These results need validating with national data to confirm these conclusions.

KEYWORDS

COVID-19, orthopaedic oncology, sarcoma

1 | INTRODUCTION

The emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has placed unprecedented pressures on healthcare systems worldwide.[1] A balance has been needed between the risk of nosocomial acquired coronavirus and the risk of progression and metastasis due to treatment delay. Surgical cancer care poses a unique challenge as delayed diagnosis and definitive treatment will undoubtedly result in a worse prognosis. The role of neo-adjuvant treatments including radiotherapy and chemotherapy and their safe administration within the confines of safe practice during the peak of the pandemic must also be balanced against the perceived optimum treatment for primary malignancies.

The safe administration of surgical care has, again, posed unique challenges due to the risk of disease transmission in the operating theatre environment. The need for high numbers of staff to support safe care, as well as the high-risk aerosol generating procedures incumbent on delivering safe surgery, has tested surgical healthcare worldwide.

At the outset of the pandemic, the majority of institutions suspended elective procedures in an attempt to reduce footfalls in hospitals, manage patient flow and ensure capacity for nonelective, urgent or emergent care. However, within this context, the maintenance of safe surgical care for patients with cancer has been maintained where appropriate. Malignant disease where surgery forms the mainstay of treatment, including bone and soft-tissue sarcoma care, have been maintained during the pandemic, with modifications in pathways and attempts to minimise the risk to patients of contracting coronavirus during the peri-operative phase. Individual institutions have developed solutions particular to their environment and the patient cohort requiring treatment.

Our specialist orthopaedic hospital delivers all aspects of orthopaedic care including specialist orthopaedic oncology care. At the outset of the pandemic, the trust developed a framework to deliver risk managed care for patients with primary malignant conditions of bone and soft tissue, as well as metastatic bone disease. The aim of this study is to report the incidence of SARS-CoV-2 during and up to 14 days post-discharge, respiratory complications and 30-day mortality in orthopaedic oncology patients during the SARS-CoV-2 pandemic.

2 | METHODS

After institutional approval, we performed a prospective observational cohort study of all patients admitted to a single United Kingdom hospital during the SARS-CoV-2 pandemic to date to undergo urgent orthopaedic oncology surgery. Due to the pandemic, we did not directly include patient nor public involvement in this study. All patients were aged 16 years or older and underwent surgical procedures for bone or soft-tissue sarcomas, giant cell tumours of bone, metastatic bone disease or plastic surgical procedures as a result of limb-salvage surgery. Where patients had multiple operations during their admission the date of surgery was taken as the first procedure.

A risk assessment for each patient was conducted on a case by case basis taking into consideration patient and diagnostic factors. All cases were discussed in a specialist orthopaedic oncology multidisciplinary team meeting before admission. Patients were considered appropriate for surgical intervention during the pandemic where the surgical plan was at a timepoint dictated by neo-adjuvant chemotherapy or radiotherapy, where neo-adjuvant treatment was not possible and the risk of disease progression without intervention outweighed the predicted risk of nosocomial coronavirus transmission, or where delay in surgical treatment would have incurred a significant risk to life or limb. Patients were screened for symptoms of SARS-CoV-2 before admission via telephone. No formal swab or antibody screening was undertaken before admission, except for patients transferred from other hospitals, but in the presence of symptoms, patients were delayed until symptom resolution. All patients were nursed on a single ring-fenced ward. Nursing staff remained on this ward throughout the period of study and cross cover for other non-ring-fenced wards was not allowed. Patients were admitted 24 hours before the planned surgical date to allow in hospital ***preoperative assessment. All procedures were undertaken in one of two ring-fenced operating theatres. All theatre staff including surgical teams complied with recommended guidelines for the use of personal protective equipment.

When required, patients were recovered in a high dependence level 2 unit before transfer back to the ward. In all cases, patients were discharged to their normal place of residence. On discharge, patients were informed of the need to self-isolate together with all members of the same household. Patients were phoned 14 days after discharge to discover whether the patient had developed symptoms of SARS-CoV-2 since discharge and whether they had SARS-CoV-2 confirmed using reverse-transcription polymerase chain reaction (RT-PCR) testing. Follow up arrangements were on a patient by patient basis with telephone consultations where possible. Where appropriate, patients were recommenced on adjuvant chemotherapy or were considered for adjuvant radiotherapy on the basis of recommendations from the multidisciplinary team.

The demographic variables recorded included age, sex, and American Society of Anaesthesiologists (ASA) physical status classification. Age was collected as a continuous variable and categorised into age groups. Oncological variables including diagnosis, comorbidities, smoking status and surgical procedure were recorded. Diagnosis was confirmed at the bone and soft-tissue sarcoma multidisciplinary team meeting. The diagnosis of SARS-CoV-2 diagnosis was logged as either preoperative or postoperative and made using nasal swabs and RT-PCR. Pulmonary complications were defined as pneumonia, acute respiratory distress syndrome, or unexpected postoperative ventilation as the most frequent coronavirus disease-2019 (COVID-19)-related pulmonary complications. Healthcare evaluation data (HED) is an online system allowing comparison of hospitals across the country. HED data for our department for the last 5 years were retrospectively interrogated to analyse our pre-pandemic 30-day mortality. The prevalence of COVID-19 was during the study time period was obtained from UK government national weekly COVID-19 summary reports for the study period.

3 | RESULTS

This analysis includes 100 patients admitted for surgery between 4th March 2020 and 22nd May 2020 and who have been discharged since 24th March 2020. There were 35 female and 65 males; mean patient age was 52.4 years (range, 16-94 years). Patients were grouped according to age: <29 years (n = 16), 30 to 49 years (n = 23), 50 to 69 years (n = 38), >70 years (n = 23). There were 16 males aged greater than 70 years.

Indications for surgery included soft-tissue sarcomas (45), osteosarcoma (15), metastatic bone disease (13), chondrosarcoma (11), Giant cell tumour of bone (7), Ewing's sarcoma (2), adamantinoma (2), chordoma (1), spindle cell sarcoma of bone (1), chondroblastoma (1), fibrous dysplasia (1) and peri-prosthetic fracture (1). Ten patients were admitted shortly after cessation of neo-adjuvant chemotherapy for osteosarcoma (7), Ewing's sarcoma (2) and breast cancer (1). Five patients were admitted after neo-adjuvant radiotherapy for soft-tissue sarcoma (3) and Ewing's sarcoma (2). A total of 90 patients were treated for a malignant condition, the other ten had benign aggressive bone tumours or fractures. Surgical procedures included soft-tissue sarcoma excision ± reconstruction (38), amputation (9), primary and revision endoprosthetic replacement (26), lower-limb allograft (1) intralesional curettage of bone tumour (9), pelvic resection ± reconstruction (12), plastic surgical wound management (5).

Five patients were admitted via transfer from other hospitals, all of whom were screened negative pre-transfer at the referring centre for SARS-CoV-2. During admission 51% of patients were tested upon admission for SARS-CoV-2, due to developing symptoms of fever or cough (the former is common following major surgery). Three patients, all admitted from home, tested positive for SARS-CoV-2 during their admission, leading to cancellation of surgery in two pre-operatively diagnosed cases, both of whom were symptomatic at the time of testing. The third case tested positive postoperatively but was asymptomatic.

After 14 days post-discharge, of the remaining 97 patients, one patient developed symptoms of SARS-CoV-2, self-isolated, and was asymptomatic 4 days later. Another asymptomatic patient tested positive within 14 days of discharge and remains unaffected by the virus. Two other patients have tested negative. None of the 95 other patients developed symptoms within 14 days of discharge.

Of the five patients who developed symptoms and/or tested positive during their peri-operative pathway, four were male and one female, the mean age was 41.2 years (range, 17-75 years) and all had primary malignant bone or soft-tissue tumours and four of five had received immunosuppression pre-operatively. They represent 5% of the patients admitted for urgent surgery during the study period.

The pulmonary complication rate was 3%; one patient was diagnosed with hospital acquired pneumonia and was successfully treated with intravenous antibiotics and supportive care. Another was suspected as having an intra-operative pulmonary embolus, which was excluded and managed as pneumonia with pulmonary atelectasis due to prolonged admission before surgery with a pelvic tumour. One of the cancelled patients with pre-operatively diagnosed SARS-CoV-2 was re-admitted 2 weeks later for excision of osteosarcoma and lower-limb endoprosthetic reconstruction and was transferred to the ITU 4 days later with pulmonary complications of SARS-CoV-2 necessitating ventilation but died of respiratory failure.

The 30-day mortality was therefore 1%. For the preceding 12-month period before the COVID-19 pandemic, there were seven cases of death within 30 days equating to a departmental mortality rate of 0.2%. For the preceding 5 years, a 30-day mortality rate of 0.4% was recorded. As the HED data also includes patients admitted and discharged as day cases following biopsy, for comparison, we adjusted our mortality during the pandemic to include 75-day case biopsy cases previously excluded from analysis, equating to an adjusted 30-day mortality of 0.6%. During the period of study, the mean cumulative incidence of confirmed COVID-19 within the catchment area of the treating unit was 261.6/100 000 of the population (range, 177-386/100 000).[2]

4 | DISCUSSION

Preserving orthopaedic services during the COVID-19 pandemic has been challenging internationally.[3,4] Trauma, spinal emergencies and urgent orthopaedic oncology have continued during the pandemic, and recent landmark studies have reported 30-day mortality rates of 28.8% in orthopaedic patients.[1] Clinicians have been asked to prioritise cases using the joint Royal College of Surgeons guidance; this cohort represents the most urgent of our patients requiring urgent or emergent surgery.[5]

Males, people aged 70 years or older, those with comorbidities (ASA grades 3-5), those having cancer surgery, and those needing emergency or major surgery are reportedly the most vulnerable to adverse outcomes with SARS-CoV-2.[1] In the present study, 90% of patients were treated for a malignant bone or soft-tissue tumour, and 15% had recently completed neo-adjuvant chemotherapy or radiotherapy. As is common in orthopaedic oncology, the cohort of patients includes all age groups, only 23% were aged greater than seventy. A total of 92% of this cohort had one or more of these risk factors for adverse outcomes with SARS-CoV-2, highlighting the potential susceptibility of orthopaedic oncology patients undergoing surgery during the pandemic.

This cohort of patients represents the response of a single institution to an evolving public health emergency. Much like other specialist hospitals, the provision of elective care was suspended at the outbreak of lockdown to prevent the perceived risk to patients undergoing elective surgery and to provide capacity to the system as a whole to maintain emergency activity and flexibility for the centres providing essential support to COVID-19 patients. The plans and guidelines for patients undergoing surgery during the pandemic was developed in response to the perceived risk to patients rather than as a predictive measure before the outbreak. As such, the response represented a best guess of risk management for patients undergoing urgent orthopaedic oncology surgery. Patients were screened but not routinely tested for COVID-19 pre-operatively nor was strict self-isolation a mandatory factor before admission. Patients were admitted to and nursed on a ring-fenced specialist ward without mixing of staff between other areas of the hospital where they may have been exposed to COVID-19-positive patients. Procedures were undertaken in a ring-fenced theatre used exclusively by the oncology service during the period of the crisis. As such, all efforts were made to minimise the potential risk of exposure to the patient cohort. The

results presented here demonstrate that in spite of the lack of formal screening or isolation, patients were able to receive appropriate treatment in a timely manner in a safe environment without the incumbent risk of contracting COVID-19 during the peri-operative period and without the dramatic risk of morbidity and mortality highlighted in the evolving literature.

This study has several limitations. This cohort of patients are not directly generalisable to other subspecialities within orthopaedics, but the majority of included patients have had more extensive and longer procedures than in our elective arthroplasty practice, and 15% underwent surgery following neo-adjuvant chemoradiotherapy. Our centre is an elective orthopaedic hospital where no patients with SARS-CoV-2 were admitted for treatment of respiratory complications; however, one of the five wards was ringfenced for patients with SARS-CoV-2, as in acute trusts, and patients were admitted with fractures and spinal emergencies, some of whom tested positive for SARS-CoV-2, therefore, ours was not a COVID-19-free hospital site. Asymptomatic patients were not tested routinely preoperatively and postoperatively for SARS-CoV-2, therefore, our outcome of assessing symptoms after 14-day post-discharge may have missed some patients who were asymptomatic and had contracted the virus. This is small group of patients, being treated for rare diseases, but the limited morbidity and mortality in such a vulnerable group is encouraging for the next 100 patients.

This study has identified that high-priority orthopaedic oncology patients have not been subjected to significant additional risk during the SARS-CoV-2 pandemic. It has also underlined the risks of operating on patients with SARS-CoV-2, as 20% of the patients who had symptoms or diagnosis of COVID-19 died peri-operatively. The majority of these symptomatic or COVID-positive patients were immunosuppressed following neo-adjuvant chemotherapy or radiotherapy as part of their sarcoma treatment. As we return to normal service, preoperative screening will be crucial to identify and isolate such patients from our other vulnerable oncology patients. What this study does not add is the decision making when SARS-CoV-2 is pre-operatively identified in a sarcoma patient who could be delayed 2 weeks but not 2 months due to the hazards of disease progression.

In conclusion, with the appropriate peri-operative measures to prevent viral transmission in hospitals, major surgery for urgent orthopaedic oncology patients can continue during the COVID-19 pandemic. These results need validating with national data to confirm these conclusions.

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AUTHOR CONTRIBUTIONS

JDS: Initiated project, designed methodology, collected and analysed data, wrote the manuscript; SE, GM, RT, AA, LJ: edited the manuscript; MP: wrote the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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