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Research Article

COVID-19 related delays in diagnosis and intervention for patients with malignant bone tumours-recommendations for future pandemic planning

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Abstarct

Introduction: During the COVID-19 pandemic, UK cancer-screening services were suspended. We aimed to investigate whether COVID-19 restrictions caused delays in diagnosis and interventions for bone tumour patients.

Materials and Methods: A retrospective cohort study (2018-2020) was undertaken in patients referred to an orthopaedic department, with radiological or biopsy-proven malignancy with complete or impending pathological fractures. Patient demographics, dates of referrals and intervention were extracted from local Bony Metastasis Registry (TBMR). Minimum follow-up =18-months.

Results: The total number of orthopaedic malignancy referrals was higher in June 2020 (n=13) vs 2018 (n=4) &2019 (n=5). In 2020, time between a referral for suspected malignancy and investigation was longer than 2019 (p=0.29). Time between investigations and diagnosis was significantly less in 2020 (7±9 days, p=0.02) vs other years (28±49 days, 2018, 12.5±21.5 days, 2019). Time between medical intervention and death was less in 2020.

Discussion & Conclusions: Data suggests higher numbers of patients with new pathological lesions presented after initial UK lockdown suggesting delayed presentation. Time from referral to surgical intervention and from surgery to death was significantly reduced, suggesting missed interventional opportunities leading to increased morbidity &mortality. This highlights the impact of COVID-19 restrictions on bone tumour patients and emphasizes considerations for pandemic planning of cancer services.

Introduction

A novel coronavirus disease COVID-19, caused by severe acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2), was identified in December 2019 in Wuhan, China [1]. The rapid spread of this new, infectious virus causing a global pandemic suspended routine UK cancer screening services in March 2020 in order to divert the workforce to COVID-19 areas [2]. During this lockdown period, figures suggest that 200,000 people per week were no longer screened for bowel, breast and cervical cancer across the UK [2]. This could have left a significant number of early cancers failed to be diagnosed early. Furthermore, many primary care physicians opted for telephone or video consultations to avoid patients attending surgeries [3]. The impact of these factors on diagnosis of primary and secondary bone malignancies is unknown. Primary malignant bone tumours are

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rare, accounting for 0.2% of all cancers [4], however secondary bony metastases occur in every type of cancer and pathological fractures (i.e. fracture due to mechanical weakening of bone, in this context due to neoplastic disease) occur in up to 10% of patients [5, 6]. Even in patients with known metastatic bone disease, it is vital to detect impending fractures before they break since they can cause intractable pain, metabolic disturbance and impact upon quality of life [7, 8]. Early detection could potentially minimise the need for treatment, improve patient outcomes and make subsequent prophylactic surgery technically easier and less challenging, with better recovery, shorter operative time, less morbidity, and reduction in the length of hospital stay [7, 9].

With routine screening paused and the change of approach in primary care, it is hypothesised that the number of referrals for malignant bone lesions to our orthopaedic service was reduced due to substantial service disruption. We aimed to investigate whether the COVID-19 restrictions had caused a delay in diagnosis and interventions for bone tumour patients.

Materials and Methods

A retrospective cohort study investigating the first set of COVID-19 restrictions (01/03/2020 to 30/06/2020) was undertaken in all patients referred to an orthopaedic department with a radiological or biopsy-proven primary or secondary malignancy. All patients with a complete or impending pathological fracture were included. This group was compared to consecutive patients referred over comparable dates in 2018 and 2019 (01/03/2018-30/06/2018 and 01/03/2019-30/06/2019). Patients were excluded if they suffered an injury due to a mechanical fall. There were no upper or lower age limits and patients were followed up until death or until December 2021, whichever was latest. Patient demographics (age, gender), dates of referrals, dates of diagnostic investigations and dates of interventions (medical and surgical) were extracted from the local Bony Metastasis Registry (TBMR) database, trauma meeting lists and the regional clinical portal system. Where study groups were directly compared, dataset analysis comprised the Chi-square test for categorical variables and the student's t-test or non-parametric Wilcoxon test as appropriate for continuous variables (significance $p<0.05$).

Results

Study population

Between March and June in 2018 and 2019, 1331 and 1694 patients, respectively, were referred to a UK regional trauma centre as acute trauma referrals. Of these patients, the prevalence of suspected bone malignancy was 0.7 and 1.2%, respectively (9/1331 and 21/1694) In 2020, there was no significant difference in the percentage or absolute number of patients referred to the acute orthopaedic trauma take with suspected or proven bone malignancy (16/1452, 1.1%). (Figure 1). Overall, the mean age of patients referred was 67.9 years (range 33-92 years). The commonest diagnoses were prostate cancer accounting for 28% of cases (n = 13/46), followed by lung and breast cancer, both 22% (n = 8/46). (**Table 1**) (**Figure 2**). No primary malignancies were diagnosed. There were less breast cancer diagnoses in 2020 compared to 2019 (n=3 vs n=5), although in 2018 (n=0). The number of lung, haematological and prostate cancers diagnosed remained comparable in 2018-19-20. The number of female patients diagnosed with malignancy was 22.2% (n= 2/7) in 2018, 42.9% (n=9/21) in 2019 and 37.5% (n= 6/16) in 2020 (**Table 1**).

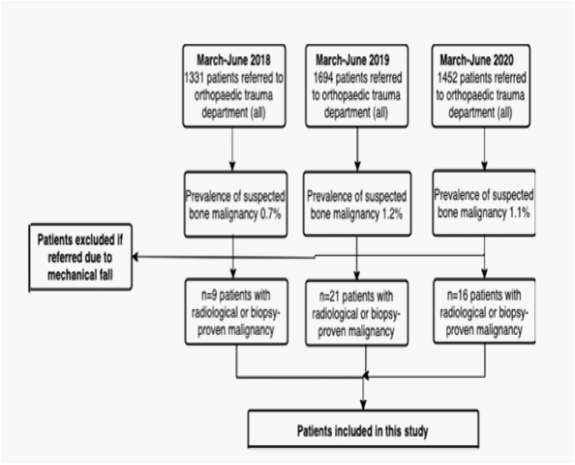

Figure 1: Flowchart summarising the patients included in this study.

Table 1: Summarising demographic data for all patients referred to Trauma and Orthopaedic department with proven malignancy and that are included in this study.

Demographic	Total n=46	2018 n=9	2019 n=21	2020 n=16
Mean age, yrs (range)	67.9 (33-92)	67.3 (54-83)	66.8 (50-98)	69.9 (51-82)
Male, n (%) Female, n (%)	29 (63.1) 17 (36.9)	7 (77.8) 2 (22.2)	12 (57.1) 9 (42.9)	10 (62.5) 6 (37.5)
Primary Cancer, n (%) Prostate Lung Breast Renal/urological Haematological Other Multiple	**n=46** 13 (28.2) 8 (17.3) 8 (17.3) 6 (13.1) 6 (13.1) 3 (6.5) 2 (4.3)	**n=9** 2 (22.2) 3 (33.4) 0 (0) 0 (0) 2 (22.2) 2 (22.2) 0 (0)	**n=21** 7 (33.3) 3 (14.3) 5 (23.8) 3 (14.3) 3 (14.3) 0 (0) 0 (0)	**n=16** 4 (25) 2 (12.5) 3 (18.7) 3 (18.7) 1 (6.3) 1 (6.3) 2 (12.5)

100% (n=5/5) of all malignancies referred to orthopaedics were new referrals in April and May 2020 (i.e. no patients presenting due to recurrence or disease progression). (**Table 2**) This contrasts with June 2020 data where 77.5% (n=7/9) of referrals were due to disease progression or reoccurrence. One patient had disease progression of 2 malignancies-prostate and bladder throughout the COVID-19 pandemic, leading to palliation and end of life care.

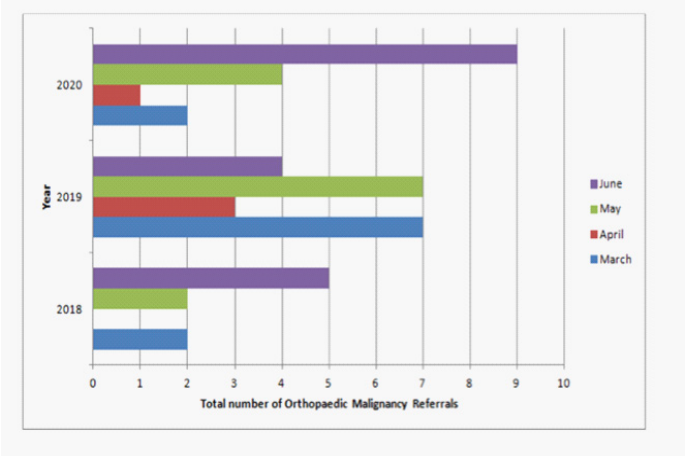

Figure 2: Chart showing the breakdown of each radiological or biopsy proven malignancy by month and year.

Table 2: Summarising data for all patients that presented with new malignancy, reoccurrence or disease progression.

	Total n=46	2018 n=9	2019 n=21	2020 n=16
New referrals				
March	4	2 (22.2)	2 (9.5%)	0 (0%)
April	2	0 (0%)	1 (4.8%)	1 (6.3%)
May	9	1 (11.1%)	4 (19%)	4 (25%)
June	3	0 (0%)	1 (4.8%)	2 (12.6%)
Reoccurrence				
March	6	0 (0%)	5 (23.8%)	1 (6.3%)
April	0	0 (0%)	0 (0%)	0 (0%)
May	1	1 (11.1%)	0 (0%)	0 (0%)
June	6	4 (44.5)	1 (4.8%)	1 (6.3%)
Disease Progression				
March	1	0 (0%)	0 (0%)	1 (6.3%)
April	2	0 (0%)	2 (9.5%)	0 (0%)
May	3	0 (0%)	3 (14.3%)	0 (0%)
June	9	1 (11.1%)	2 (9.5%)	6 (37.5%)
TOTAL N, (%)	46	9, (100%)	n = 21 (100%)	n = 16 (100%)

Diagnosis and Intervention

June 2020 saw the highest number of referrals at any time frame over the study period. (Figure 3). In 2020 the time between a referral for suspected malignancy and any investigation was substantially longer than the same period in 2019. (6.5±13.8 days, 2020, 13.5±19.3 days, 2019) (p=0.29). The time between investigations and formal diagnosis was significantly less in 2020 (7±9 days, p=0.02) vs other years (2018, 28±49 days, 2019, 12.5±21.5 days). The time between diagnosis and intervention was substantially less in 2020 (10 ±17) compared to 2018 (16±21.5 days, p=0.14) and 2019 (19±45.6 days, p=0.06) (**Table 3**).

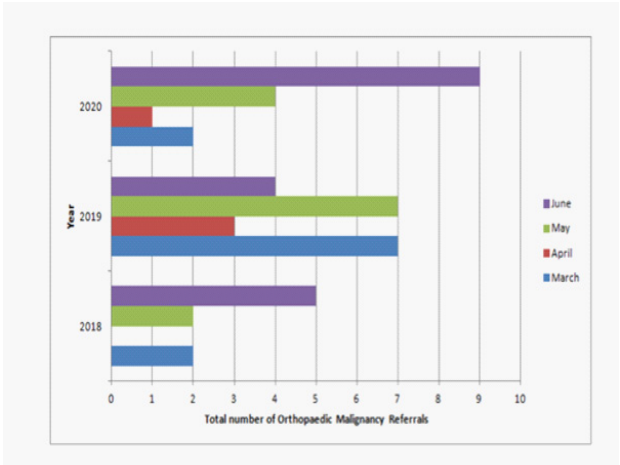

Figure 3: Bar chart showing the number of radiological or biopsy proven malignancies that were referred to an Orthopaedic department in March to June, 2018-2020. June 2020 saw the highest number of referrals across the study timeframe.

Table 3: Summarising data for the time lapses between referral, investigation, diagnosis and intervention.

	2018	2019	2019-18 (combined)	2020	P value (<0.05) *denotes significance
Time between initial referral and investigation (days) (median, IQR)	14.0±103.5	6.5±13.8	10.3±58.7	13.5±19.3	0.32
Time between investigation and diagnosis (days) (median, IQR)	28±49	12.5±21.5	20.3±35.6	7±9	0.01*
Time between diagnosis and intervention (days) (median, IQR)	16±16	19±45.6	17.5±30.8	10±17	0.02*

Progression to surgery

(**Table 4**) highlights the rates of progression to surgery in 2018-20. In 2020, only 25% (n=4/16) of patients progressed to surgery, compared to 55.5% (n=5/9) and 57.1% (n=12/21) in 2018 and 2019 respectively. The time between the patient referred to orthopaedics and any surgical intervention was less in 2020 (2±2.5 days), compared to 2018 (4.8 ± 7.9, p=0.65) and 2019 (4.5±9.5, p=0.09).

Table 4: Rates of progression and time to surgery in the study cohort.

	Year	Month				
Surgery n = 9 (n, %) n = 21 (n, %) n = 16 (n, %)	**2018** **2019** **2020**	**March** 2 (22.2) 4 (19.0) 1 (6.3)	**April** N/A 1 (4.8) 0	**May** 1 (11.1) 5 (23.8) 0	**June** 2 (22.2) 2 (9.5) 3 (18.8)	**Overall** **5 (55.5)** **12 (57.1)** **4 (25)**
Time from referral to surgery (days) (median, IQR)	**2018** **2019** **2020**	**March** 10±9 3±10.6 1	**April** N/A 32 N/A	**May** 1 5±9 N/A	**June** 1.5±0.5 11±1 3±2	**Overall** **4.8±7.9** **4.5±9.5** **2±2.5**

Mortality

30-day and 90-day mortality (from date of trauma meeting) is shown in table 5. 2020 saw the highest mortality percentage of patients at 30 and 90 days. At the end of the follow-up period (minimum 18-months) rates of mortality were comparable in 2019 and 2020, but higher in 2018 (**Table 5**).

Table 5: Summarising overall mortality data in the study cohort.

Year	30-day mortality (%)	90-day mortality (%)	18-month mortality (%)
2018 (n=9)	22	33	78
2019 (n=21)	10	14	67
2020 (n=16)	25	38	69

Discussion

The unprecedented demand on the NHS, secondary to the COVID-19 pandemic, remains problematic due to mass disruption of routine medical and surgical services. Maringe et al. [10] project a large number of additional cancer deaths due to national pandemic measures. This is echoed with delays in malignancy diagnoses and subsequent surgery causing an exponential burden of attributable mortality [11].

Data from our study suggests higher numbers of patients with new bony pathological lesions presented after the initial lockdown period in the UK. In our cohort, 100% (n=5/5) of malignancies referred to orthopaedics were new referrals in April and May 2020 which, contrasts with June 2020 data where 77.5% (n=7/9) of referrals were due to disease progression or reoccurrence. (Table 2). This concurs with data from public health Scotland that suggest there were four thousand fewer pathological diagnoses of cancer throughout the same time frame [12]. In concordance with the published literature, overall gender and primary malignancy diagnoses were comparable to previous studies [13].

In previous years (2018 and 2019), more that half of patients underwent an orthopaedic operation (either prophylactically for an impending fracture or for a fracture thorough a malignant lesion). In 2020, only 25% of patients had surgery. This figure suggests patients presented later to our services and perhaps were deemed too medically or terminally unwell to be considered for prophylactic surgery. A similar pattern has been observed in head and neck malignancy, where patients presented later and required more complex reconstructive surgery [14]. In comparison to 2018-19, the mortality rate in patients referred to the Trauma and Orthopaedic service between March and June 2020 was highest at both thirty and ninety days. These figures further suggest patients presented later to our services. However, by eighteen months, the mortality rates were comparable across the years. This may be explained by the fact we do not know how many patient patients failed to be diagnosed with a malignancy during the COVID-19 pandemic, thus not referred to our service and captured in our data collection. Data published in the BMJ suggests there were 286,000 less urgent cancer referrals from primary into secondary care [15].

The time from investigation to diagnosis and diagnosis to orthopaedic surgical intervention were significantly less in 2020. A study by Him Wang et al. [16] published that hospital admissions, orthopaedic surgery and out-patients' clinics for our speciality was decreased. This suggests those patients needing surgery that presented to our department, could get an operation in a faster timeframe with the necessary pre-operative investigations completed, as highlighted in our data.

We acknowledge the limitations of our study; as there are small numbers of patients in a single tertiary centre, which may not account for regional variations and risk type II error.

Conclusion

In conclusion, due to COVID-19, we note patients with metastatic malignancy presented later to secondary care, resulting in higher rates of mortality at both thirty- and ninety-days post-presentation to the Orthopaedic department. At this stage the disease process is more advanced, the patient is more likely to be more systematically compromised and hence less likely to undergo surgical intervention of lesions at risk of pathological fracture. With new variants emerging and no imminent signs of returning to pre COVID-19 services, we recommend patients with metastatic bony disease are referred early to an Orthopaedic service, in order to consider prophylactic surgery before they are medically unfit for surgical intervention.

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Conflict Of Interest: The Authors declare that there is no conflict of interest.

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