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ORIGINAL ARTICLE

30-day mortality for fractured neck of femur patients with concurrent COVID-19 infection

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Abstract
Introduction Risk factors for mortality associated with COVID-19 have been reported to include increased age, male sex and certain comorbidities. Fracture neck of femur (NOF) patients is high-risk surgical patients, often with multiple comorbidities and advanced age. We quantify the 30-day mortality rate in fractured NOF patients with a positive peri-operative COVID-19 antigen test and identify risk factors for increased mortality.
Methods This is a retrospective multi-centre review of all patients admitted with a fractured NOF and a confirmed laboratory diagnosis of COVID-19 between 1 March and 26 April 2020. Demographic data, comorbidities, ASA grade and date of death (if applicable) were collected.
Results There were 64 patients in the cohort with an overall 30-day mortality rate of 32.8% ($n=21$). Thirty-five (55%) were female, and mean age was 83 (SD 9, range 46–100) years. There was significantly increased mortality for those with a history of myocardial infarction ($p=0.03$). Sixty-four percent of patients underwent surgery within the 36-h target, which is comparable to previous data for the same time of year. Overall mortality increased to 50% ($n=32$) at 45 days post-operatively.
Conclusion This is a large review of 30-day mortality in NOF patients with concurrent COVID-19 infection. We report a substantial increase from the pre-COVID-19 mean 30-day mortality rate (6.5% in 2019). We highlight the need for counselling patients when presenting with a NOF in relation to peri-operative COVID-19 infection and the associated increased risks.

Keywords COVID-19 · SARS-CoV-2 · Fractured neck of femur · Mortality · Hip fracture

Introduction

The COVID-19 pandemic has had a dramatic impact on the United Kingdom's National Health Service (NHS) in recent months. However, despite unprecedented social restrictions during the pandemic, we have continued to see fragility hip fracture admissions, and we assume due to the majority of these injuries occurring in the patients' normal place of residence [1, 2]. In the UK in 2018, there were over 66,000 hip fractures registered with the National Hip Fracture Database (NHFD) with a 30-day and 1-year mortality rate of 6.1% and 33%, respectively [3].

Fragility hip fracture patients are often frail, with high American Society of Anaesthesiologists (ASA) grades [4, 5]. In 2015, only 2.1% of patents presenting with a hip fracture were ASA grade 1, with the majority being ASA grade 3 (56.8%) [6]. National Institute of Clinical Excellence (NICE) clinical guidance (CG124) states that patients should have definitive surgery on the day of, or the day after diagnosis,

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along with other criteria, aiming to reduce mortality and morbidity [7].

Risk factors for increased mortality associated with COVID-19 infection have been reported. These include older age, cardiovascular and chronic respiratory disease, diabetes mellitus, hypertension, obesity, black or South Asian identity, male sex and cancer [8–11]. Many of these comorbidities are prevalent amongst patients presenting with a fractured neck of femur (NOF) [12].

Early studies have examined mortality in fractured neck of femur patients with concurrent COVID-19 infection. A multi-centre study from Hubei Province, China, reviewed ten patients undergoing surgery for various fractures (including six neck of femur fractures) with a concurrent diagnosis of COVID-19 and reported a mortality rate of 40% [13]. An Italian study specifically looking at COVID-19 positive fractured neck of femur patients reported a mortality rate of 44% of 16 patients at 7-day follow-up [14]. Data from a Spanish multi-centre study demonstrated a mortality rate of 34% amongst 23 COVID-19 positive hip fracture patients at a mean follow-up of 14 days [15]. A fourth study reviewing in-patient mortality in fractured neck of femur patients during the height of the COVID-19 outbreak in New York reported a mortality rate of 55% amongst nine patients who tested positive for COVID-19 with 21-day follow-up [16]. All studies show a markedly increased mortality rate than expected for fractured neck of femur patients when comparing to previous UK data, via the NHFD.

In this retrospective multi-centre review, we aim to quantify the 30-day mortality rate in patients presenting with a fractured neck of femur and a concurrent diagnosis of COVID-19 based on a positive antigen test and identify risk factors for increased mortality. We hypothesise that concurrent COVID-19 infection will increase 30-day mortality rate for fractured neck of femur patients.

Methods

Study design

This was a multi-centre retrospective study carried out across ten trauma units in the UK.

Participants

All patients aged ≥ 60 admitted between 1 March 2020 and 26 April 2020 with a diagnosis of a fractured neck of femur, and a confirmed COVID-19 infection, by detection of SARS-CoV-2 on quantitative RT-PCR on respiratory tract samples pre-operatively, or within 30 days post-operatively, were identified and included in the study. Included fracture types were those classified as “hip fractures” by the National Hip Fracture database: displaced intracapsular, undisplaced intracapsular, grade A1/A2 trochanteric, grade A3 trochanteric (including reverse oblique) and subtrochanteric [3]. Midshaft/distal femoral fractures, periprosthetic fractures and polytrauma patients were excluded.

Data collection

Data were collected retrospectively by review of patient notes and radiographic imaging. Patient demographics, including date of birth, ethnicity (in line with The Office of National Statistics guidelines) and sex, were recorded [17]. Date and time of radiological fracture diagnosis, date of positive COVID-19 antigen test date, date, time and type of surgery (if applicable) and date of death (if applicable) were recorded. Comorbidities incorporated in the Charlson Comorbidity Index and ASA grade were also recorded [18].

Statistical analysis

Continuous variables were presented as means, with standard deviation and range. Comparison was made using unpaired *t*-tests between survival and non-survival groups at 30 days post-fracture diagnosis. Categorical variables were presented as frequencies with percentages, and comparison was made using Fisher’s exact test between survival and non-survival groups at 30-day post-fracture diagnosis. A two-sided p value ≤ 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 25.0 (IBM, Armonk, New York).

Results

Demographics

In total, 64 patients met the eligibility criteria. Data were collected for all 64 patients, 29 (45%) were male and 35 (55%) were female. The mean age in our cohort was 83 years (SD 9.35, range 46–100). The majority of patients were white (including English, Welsh, Scottish, Northern Irish, British Irish, Gypsy or Irish Traveller and any other White background) at 97%, whilst 3% of patients were Asian/Asian British (including Indian, Pakistani, Bangladeshi, Chinese and any other Asian background). There were no patients in any of the other ethnic background categories. Demographics of patients included in the study can be seen in Table 1.

Table 1 Characteristics of patients with NOF fracture and confirmed COVID-19 infection

	n (%)			
	Total ($n=64$)	Survived 30 days ($n=43$)	Died at < 30 days ($n=21$)	*p* value*
Age, mean, (SD)	83 (9)	82 (11)	84 (6)	0.43
Gender				
Male	29 (45)	17 (40)	12 (57)	0.29
Female	35 (55)	26 (60)	9 (43)	0.29
*Comorbidity***				
Charlson score, mean, (SD)	6 (3)	6 (3)	6 (2)	0.77
MI	11 (17)	4 (9)	7 (33)	0.03
CCF	14 (22)	9 (21)	5 (24)	1.00
Dementia	27 (42)	21 (49)	6 (29)	0.18
Cerebrovascular disease	10 (16)	7 (16)	3 (14)	1.00
Chronic lung disease	12 (19)	7 (16)	5 (24)	0.51
Diabetes	17 (27)	11 (26)	6 (29)	1.00
Moderate or severe kidney disease	15 (23)	10 (23)	5 (24)	1.00
Tumour	8 (13)	7 (16)	1 (5)	0.25
Management				
Surgical	58 (91)	41 (95)	17 (81)	0.08
Conservative	6 (9)	2 (5)	4 (19)	0.08

**p* value denotes difference between patients who survived 30 days and those who died at < 30 days of injury

**Comorbidities with a prevalence < 5 have been excluded from the table

Comorbidities

Charlson Comorbidity Index was calculated for each patient, the mean score was 6, and the modal score was 5. Most common comorbidities recorded were dementia ($n=28$, 39%) followed by diabetes mellitus (DM) ($n=20$, 28%), moderate or severe kidney disease ($n=17$, 24%) and congestive cardiac failure (CCF) ($n=15$, 21%).

Diagnosis of COVID-19

In all trauma units at the time of the study, only symptomatic patients were being tested for COVID-19. In most cases, a diagnosis of COVID-19 was confirmed on antigen testing after the diagnosis of fracture was made. Three patients (5%) had a positive COVID-19 antigen test results prior to diagnosis of fracture (≤ 7 days prior to fracture), nine patients (14%) had their positive test on the same day of the fracture, and 52 patients (81%) at least 1 day following fracture diagnosis.

Diagnosis and management of hip fracture

The majority of the hip fractures were intracapsular: thirty-one displaced and five undisplaced. Twenty-three were intertrochanteric type A1/2, three were intertrochanteric type A3, and two were subtrochanteric neck of femur fractures.

The majority of patients underwent surgical intervention ($n=58$, 91%). Six patients (9%) were managed conservatively. Of these six patients, five were deemed unfit for surgery, and one patient refused surgery. Of those treated surgically, thirty underwent fixation (twenty dynamic hip screws, eight intramedullary nails and one cannulated hip screws). The remaining operative patients received a hemi-arthroplasty ($n=29$).

Of the patients who underwent surgery, one (2%) was classified as ASA grade I, five (9%) were ASA grade II, 32 (56%) were ASA grade III, and nineteen (33%) were ASA grade IV. No patients were classified as ASA grade V or VI. The target of surgery within 36 h of diagnosis or time of injury, for those who sustain injuries in hospital, as set out in the best practice tariff, was achieved by thirty-seven (64%) patients.

Mortality

The mortality rate for all patients at 30-day post-fracture diagnosis was 32.8% ($n=21$). Of the 58 patients treated surgically, 17 of these died (29%) within 30 days. Of the six patients treated conservatively, four died within 30 days; the remainder of those treated conservatively died within 45-day

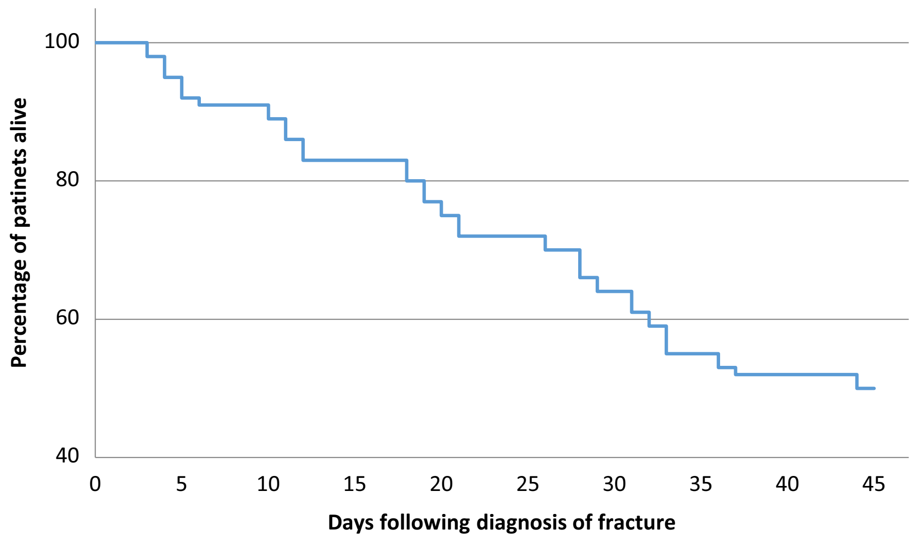

Fig. 1 Survival analysis

post-injury. The total mortality rate increased to 50% at 45 days post-operatively ($n = 32$), and this is seen in the survival analysis chart (Fig. 1).

The mean age of patients who died within 30 days following fracture diagnosis was 84, and those that survived was 82; this difference was not of statistical significance ($p = 0.43$). Thirty-day mortality for males was 41.4% compared to 25.7% for females; however, this was not a statistically significant difference ($p = 0.29$). There was no difference in the Charlson Comorbidity Index score of patients who died within 30 days following injury and those who survived ($p = 0.77$); however, 30-day mortality was greater for patients with a history of myocardial infarction (MI) ($p = 0.03$).

Discussion

We believe this is one of the largest studies of 30-day mortality in fractured neck of femur patients testing positive for COVID-19 infection to date. We report a mortality rate of 32.8% at 30-day post-injury.

Thirty-day mortality rate, for patients with a fractured neck of femur, are audited nationally through the national hip fracture database (NHFD) in the UK. Of the 66,000 neck of femur fracture patients in 2018, the overall 30-day mortality rate was 6.1% [3]. There are, however, seasonal variations in mortality rate associated with hip fractures, and previous data show higher mortality in the winter months (6.7% mortality rate in July to a peak of 8.7% in January) [3]. Mean mortality rates from the previous 4 years (2016–2019) for the months of March and April were 6.75% and 6.8%, respectively [1]. Data are also available for individual hospitals, up to February 2020. Mortality rate at 30 days for 2019 ranged from 4.2 to 8.6% for the ten hospitals in this study [1]. The 30-day mortality rate of 30.8% is similar to other international studies reporting on COVID-19 positive fractured neck of femur patients, which varies between 34 and 55% [14–16]. These were studies with fewer COVID-19 positive patients and did not report on 30-day mortality rate specifically.

The overall mortality rate for COVID-19 infection is not known, due to lack of testing of those with mild symptoms [19]. However, the World Health Organisation has reported that of those who have tested positive worldwide, 6.9% have died [20]. In hospital, mortality rates have varied in the literature from 15 to 28.5% [13–16, 21–23]. A recent UK study of 16,749 patients admitted to hospital with COVID-19 reports a mortality rate of 31% for patients with a ward-based level of care [10].

COVID-19 mortality varies with patient age, comorbid status, sex and ethnicity. Increased age, male sex, cardiovascular disease, respiratory disease, hypertension and obesity have been stated as risk factors for high mortality with COVID-19 [8, 10, 11]. In England and Wales, 73% of COVID-19-related deaths have been in patients aged 75 and over [24]. An Italian study looking at 1625 deaths from COVID-19 has reported case fatality rates of 3.5% for patients aged 65–69, jumping to 12.8% for those aged 70–79, increasing further to 20.8% in those aged 80 and over [25].

Our results similarly demonstrate that in patients with a fracture neck of femur and concurrent COVID-19 diagnosis, patients with cardiovascular disease (previous MI) were at an increased risk of death. Although we reported a greater mortality rate in males than females (41.4% compared to 25.7%), this was not of statistical significance, which we hypothesise is due to the small sample size.

Charlson Comorbidity Index scores were not demonstrated to be an indicator for increased mortality, neither were any of the individual comorbidities that make up the score other than previous MI. Mean Charlson Comorbidity Index scores of 6 fit with mean scores in the literature suggesting our cohort were no more unwell than a typical neck of femur patient [5, 12].

Six patients (9%) were treated conservatively, which is higher than expected. In 2019, only 2.3% of hip fracture patients were treated conservatively [26]. Of our conservatively treated patients, five were deemed not fit for surgery and one patient refused surgery. A larger data series would be necessary to draw further conclusions from this.

Delays to theatre are known to increase mortality amongst fractured neck of femur patients. Best Practice Tariff Guidelines in the UK mandate that definitive surgical fixation should occur within 36 h from admission to hospital, or diagnosis if fracture occurs whilst an inpatient [27]. Despite the COVID-19 pandemic, of the patients treated surgically in this study, 64% underwent definitive surgery within the 36-h target, which is comparable to the national data for the same time of year for the previous 4 years. The mean percentage of patients nationally having definitive surgery within 36 h in March and April 2016–2019 was 60.1% and 58%, respectively [1]. Therefore, these results suggest that increased mortality in fractured neck of femur patients with COVID-19 was not due to delays to theatre.

During data analysis, it became apparent that a substantial number of patients died after the 30-day benchmark. To explore this, we extended the survival analysis to 45 days (Fig. 1). Mortality rate in this group was 50%, 100% in those treated conservatively ($n = 6$) and 44.8% in those treated surgically $n = 26$). These findings cannot be compared to 30-day mortality. The NHFD currently records fractured neck of femur mortality at 30 and 120 days (30 days and at 1 year prior to 2019). To our knowledge, this pattern of increased mortality to 45 days has not previously been recognised, and we postulate COVID-19 infection as the cause for this in our patient demographic. Mortality rates in 2017 at 1 year were 33% which are already surpassed in our COVID positive patient group at 45 days. We intend to follow up our patient group to 120-day and 1-year post-fracture, in order to make further comparisons.

Limitations

Current antigen testing has a sensitivity of approximately 70% [28, 29]. This study included only patients with confirmed positive COVID-19 antigen tests. Therefore, it is possible that some patients will have been inadvertently excluded from the study if they had a false-negative test. We only assessed COVID-19 positive patients and used previous years' data to compare mortality rates. We accept that this is a limitation of the study, and COVID-19 negative neck of femur patients presenting at the same time would be the most appropriate control group. However, we argue that because of false-negatives, and asymptomatic patients not being tested at the time of this study across all trauma units, this comparison could be compromised. There is the potential that overall care could have been negatively affected during the pandemic. Services could have been reduced, due to staff sickness, for example orthogeriatric or physiotherapy. Fewer anaesthetic and surgical team members may have been available to conduct surgery, although this has not been our experience. Time to theatre in our cohort of patient remains similar to previous years, an indicator of adequate theatre capacity. By comparing to previous year's data, we eliminate these other potential variables, whilst accepting that this is a weakness of the methodology of this paper.

The UK government enforced social restrictions on the public during the time that our cohort of patients were admitted. Thus, selection bias may affect our results, with a greater proportion of patients who fall at home and are therefore frailer, within our cohort. However, data from the NHFD states that 56% of patients who underwent operations in 2015 were ASA 3, the same as our surgical cohort [6].

Finally, increased mortality rates have been reported in the UK amongst patients of black and South Asian ethnic origin [10, 11]. However, due to a small number of patients falling into these categories (two patients of South Asian ethnic origin) we are unable to draw conclusions on whether ethnicity has an impact on 30-day mortality for fractured neck of femur patients with COVID-19.

Conclusion

This study demonstrates that fractured neck of femur patients with concurrent COVID-19 infection have a high 30-day mortality rate of 32.8%. This is a substantial increase in mortality from the national data prior to the pandemic (6.5%). It is important that clinicians are aware of this high mortality rate when counselling patients and relatives of those admitted with hip fractures. Further work is required to evaluate the impact of COVID-19 infection on mortality in other areas of surgical practice, including elective operating.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

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