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HIP



Impact of COVID-19 on clinical outcomes for patients with fractured hip

A MULTICENTRE OBSERVATIONAL COHORT STUDY

Aims

There are reports of a marked increase in perioperative mortality in patients admitted to hospital with a fractured hip during the COVID-19 pandemic in the UK, USA, Spain, and Italy. Our study aims to describe the risk of mortality among patients with a fractured neck of femur in England during the early stages of the COVID-19 pandemic.

Methods

We completed a multicentre cohort study across ten hospitals in England. Data were collected from 1 March 2020 to 6 April 2020, during which period the World Health Organization (WHO) declared COVID-19 to be a pandemic. Patients \geq 60 years of age admitted with hip fracture and a minimum follow-up of 30 days were included for analysis. Primary outcome of interest was mortality at 30 days post-surgery or postadmission in nonoperative patients. Secondary outcomes included length of hospital stay and discharge destination.

Results

In total, 404 patients were included for final analysis with a COVID-19 diagnosis being made in 114 (28.2%) patients. Overall, 30-day mortality stood at 14.4% (n = 58). The COVID-19 cohort experienced a mortality rate of 32.5% (37/114) compared to 7.2% (21/290) in the non-COVID cohort (p < 0.001). In adjusted analysis, 30-day mortality was greatest in patients who were confirmed to have COVID-19 (odds ratio (OR) 5.64, 95% confidence interval (CI) 2.95 to 10.80; p < 0.001) with an adjusted excess risk of 20%, male sex (OR 2.69, 95% CI 1.37 to 5.29; p = 0.004) and in patients with \geq two comorbidities (OR 4.68, CI 1.5 to 14.61; p = 0.008). Length of stay was also extended in the COVID-19 cohort, on average spending 17.6 days as an inpatient versus 12.04 days in the non-COVID-19 group (p < 0.001).

Conclusion

This study demonstrates that patients who sustain a neck of femur fracture in combination with COVID-19 diagnosis have a significantly higher risk of mortality than would be normally expected.

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Keywords: Hip fracture, Neck of femur fracture, NOF, Coronavirus, COVID-19

Introduction

Despite a nationally imposed lockdown in the UK to combat COVID-19, the number of elderly patients admitted to hospital with fractured neck of femur (NOF) has remained fairly consistent^{1,2} The most recent report from the National Hip Fracture Database for England, Wales and Northern Ireland concluded that for the year 2018 there were 66,140 hip fractures, with an annualized 30-day mortality of 6.1% across 175 trusts.³ Many patients who sustain a fractured NOF live in institutional care, where there is considerable risk of COVID-19 infection.⁴

Trauma teams from the USA, Spain, Italy, and regions of the UK have all published their preliminary data on the effect COVID-19 has had on patients with fractured NOF, with all observing a marked increase in perioperative mortality.⁵⁻⁹ The team from the USA⁵ included 136 NOF fracture patients from seven emergency departments in the city and county

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Bone Joint Open 2020;1-11:697– 705. of New York. Of these, 31 were deemed COVID-19 positive with 11 (34.5%) patients not surviving beyond 30 days post-surgery. Similar mortality figures among their respective COVID-19 positive cohorts were observed by the Spanish (30.4%, 7/23) and Italian (43.75%, 4/31) teams.^{6,7} Within the UK, regional teams have published their own cohort results, identifying the prevalence of COVID-19 to range from 19.4% (82/422) in London to 8.5% (27/317) in Scotland, with 30-day mortality rates of 30.5% (25/82) and 33.3% (9/27), respectively.^{8,9}

This study aims to understand the perioperative clinical outcome for elderly patients admitted to hospital with NOF fracture during the COVID-19 pandemic in the UK. Our primary objectives were to report the 30-day mortality for patients admitted to hospital with a fractured NOF and report the prevalence of COVID-19 in this same cohort.

Methods

This was a multicentre observational cohort study involving a collaboration between ten orthopaedic units within England, with the region of West Midlands supplying majority of centres (Supplementary Table i).

Local collaborators from each centre collected data both retrospectively and prospectively from the 1 March 2020 to 6 April 2020. The ten centres see approximately 3,775 patients per year and so we anticipated 400 to 435 patients in the study period. Patients were identified from handover lists, theatre operating, and local hospital digital systems. Patients \geq 60 years of age admitted to ten hospitals who had sustained a fractured NOF were included in the study. We excluded patients with pelvic fractures, femoral shafts fractures and periprosthetic fractures.

Ethics. The study was registered with the research and audit department of each participating UK centre. As we were using routinely collected anonymized data, formal research ethics approval was not required. We used the online National Research Ethics Service decision tool (http://www.hra-decisiontools.org.uk) to confirm this.

Outcomes. Primary outcome was mortality at 30 days post-surgery. In addition to this, patients were followed up throughout their hospital stay in order to determine two cohorts. The COVID-19 cohort was based on either a positive virology test (SARS-CoV-2 RNA reverse transcription polymerase chain reaction (RT-PCR) detection), or suspected signs, symptoms of COVID-19 and/or imaging (chest radiograph or CT). The non-COVID-19 cohort was based on either a negative virology test (SARS-CoV-2 RNA RT-PCR detection) or not fulfilling the Public Health England (PHE) criteria required for COVID-19 testing (applicable to all NHS hospitals during the time of this study).

Patients. We obtained data from ten centres which entered 433 patients. Of these, 404 patients met our

inclusion criteria. COVID-19 diagnosis was made in 114 patients (28.2%), with 109 RT-PCR confirmations (27%), while five patients (1.2%) had their diagnosis confirmed from clinical signs and imaging. Fifty patients (12.4%) had negative RT-PCR results whereas 245 patients (60.6%) did not meet PHE criteria for testing (Figure 1).

Confounding variables. We collected the following variables: age, sex, type of fracture, type of surgery, type of anaesthesia, ASA (American Society of Anasthesiologists) grading, and side of injury. We also collected variables needed to calculate the Nottingham Hip Fracture Score (NHFS); admission haemoglobin (Hb), pre-admission living status, history of malignancy, Abbreviated Mental Test Score (AMTS), and number of comorbidities.¹⁰ The variables were input on a predesigned database and only those with < 20% missing data were reported within this study. In addition to this, the National Hip Fracture Database was accessed by each institution and patients cross referenced for data completion.

Statistical analysis. Data are reported in accordance with Strengthening The Reporting of Observational studies in Epidemiology guidelines for Observational Studies and Statistical Analyses and Methods in the Published Literature guidelines.¹¹ Data were summarized using descriptive statistics including count and percentages for categorical variables. Continuous variables were described using the mean and SD. To test for differences in variables and outcomes, we used chisquared and Fisher's exact test for categorical variables and Mann-Whitney U test for continuous variables as appropriate. A multivariate logistic regression model was fitted to assess the impact of COVID-19 on mortality at 30 days while adjusting for potential confounders. The variables included in the multivariate logistic regression model were selected based on the statistically significant results of univariate logistic regression model including only one potential predictor. Adjusted excess mortality rate was obtained as the difference of the averages of the predicted mortality probabilities of the adjusted model assuming all patients had COVID-19 and assuming they did not have COVID-19. A two-sided p-value of < 0.05 was considered statistically significant. All analysis were performed using IBM SPSS v. 26 (Armonk, New York, USA) software for Mac.¹²

Results

Cohort characteristics. Patients with a diagnosis of COVID-19 tended to be older (mean age 85.16 years (SD 8.67) vs 82.88 years (SD 8.59); p = 0.017, Mann-Whitney U test), had larger proportion of males (37.7% (n = 43) vs 27.6% (n = 80); p = 0.046, chi-squared test), were more likely to come from institutional care (26.3% (n = 30) vs 20.3% (n = 59); p = 0.038, chi-squared test), as well as obtain higher mean ASA (3.16 (SD 0.68) vs 3.01 (0.63); p = 0.04, Mann-Whitney U test) and mean



Flow diagram depicting included patients for analysis. RT-PCR, reverse transcription polymerase chain reaction.

NHFS (5.51 (SD 1.5) vs 5.08 (SD 1.54); p = 0.012, Mann-Whitney U test) scores. While surgical interventions between the two groups proved similar, it was noted that the two cohorts had equal distribution of patients managed non-operatively. Table I describes the other variables collected among further sub grouping for age, time to surgery, AMTS, ASA, NHFS, of which none demonstrated statistical significance between the cohorts.

Clinical outcomes. Table II demonstrates significant differences in 30-day postoperative mortality between the two groups. Overall, 58 patients (14.4%) did not survive beyond 30 days postoperatively, with the majority of these being in the COVID-19 cohort group (32.5% vs 7.2%; p = < 0.001). Conversely, most (48/58) of the deaths occurred while patients were still in a hospital. The mean length of stay was 17.66 days (SD 11.16), which proved five days longer in the COVID-19 group when compared to the non-COVID-19 group. In terms of timing to COVID-19 status (i.e. positive or negative

result), in those that were tested this occurred predominantly in the postoperative period (mean 9.23 days post-surgery (SD 8.06; -4 to 30). However, 15 patients underwent testing prior to their operation with five of them recording a positive COVID-19 result.

Modalities used to confirm COVID-19 status. Table III, which corresponds to Figure 1, separates the different methods used to confirm COVID-19 status and their effects on mortality, revealing that patients who were confirmed positive by RT-PCR (31.2%; n = 34) had a significantly higher risk of death compared to negative (16%; n = 8) and not tested cohorts (5.4%; n = 13; p = 0.015, Fisher's exact test).

Predictors of outcome. Patients with a proven positive or suspected COVID-19 diagnosis had almost a six fold increased odds of mortality (OR = 5.64, 95% Cl 2.95 to 10.80, p < 0.001) and an adjusted excess risk of 20% (Supplementary Table ii). Likewise, when adjusted analysis was made to include the same significant unadjusted covariates, the only predictors that remained relevant Table I. Characteristics for COVID-19 status.

		COVID-19	Non-COVID-19	
Variable	Total	(n = 114)	(n = 290)	p-value
Mean age, yrs (SD)	83.52 (8.66)	85.16 (8.67)	82.88 (8.59)	0.017*
Age, n (%)				
< 85	194 (48)	44 (38.6)	150 (51.7)	0.017†
≥ 85	210 (52)	70 (61.4)	140 (48.3)	
Sex, n (%)				
Male	123 (30.4)	43 (37.7)	80 (27.6)	0.046†
Female	281 (69.6)	71 (62.3)	210 (72.4)	
NOF type, n (%)				
Extracapsular	206 (51)	53 (46.5)	153 (52.8)	0.257†
Intracapsular	198 (49)	61 (53.5)	137 (47.2)	
Side of injury n (%)				
Right	191 (47)	58 (50.9)	133 (45.9)	0.376†
Left	209 (52)	54 (47.4)	155 (53.4)	
Unknown	4(1)	2 (1.8)	2 (0.7)	
Pre-admission				
(%)				
Home	309 (76.5)	80 (70.2)	229 (79)	0.038†
Institution	89 (22)	30 (26.3)	59 (20.3)	
Unknown	6 (1.5)	4 (3.5)	2 (0.7)	
Mean AMTS	7.09 (3.49)	6.58 (3.92)	7.27 (3.31)	0.086*
(SD)		0.30 (3.72)	,, <u>,</u> ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	0.000
AWI 3, II (%)	252 ((2 ()	(= (= 7)	100 ((1 0)	0.0714
21	233 (02.0)	28 (22 2)	100 (04.0)	0.0711
≤ 0	120 (31.7)	38 (33.3)	90 (31)	
	23 (5.7)	11 (9.6)	12 (4.1)	0.040*
Mean ASA grade	3.06 (0.65)	3.16 (0.68)	3.01 (0.63)	0.040^
ASA grade, n (%)				
1	4 (1)	1 (0.9)	3 (1)	0.196†
2	54 (13.7)	12 (10.5)	42 (14.5)	
3	257 (65.2)	76 (66.7)	181 (62.4)	
4	75 (19)	30 (26.3)	45 (15.5)	
5	3 (0.8)	1 (0.9)	2 (0.7)	
6	1 (0.3)	1 (0.9)	0 (0)	
1 to 2	58 (14.4)	12 (10.5)	46 (15.9)	0.293†
3+	336 (83.2)	98 (86)	238 (82.1)	
Unknown	10 (2.5)	4 (3.5)	6 (2.1)	
Mean NHFS (SD)	5.2 (1.54)	5.51 (1.5)	5.08 (1.54)	0.012*
NHFS, n (%)				
≤ 5	219 (54.2)	57 (50)	162 (55.9)	0.287†
≥ 6	185 (45.8)	57 (50)	128 (44.1)	
Malignancy, n (%)				
Yes	52 (13)	12 (10.5)	40 (13.8)	0.368†
No	347 (86)	101 (88.6)	246 (84.8)	
Unknown	5 (1)	1 (0.9)	4 (1.4)	
Preoperative Hb < 100, n (%)				
Yes	50 (12)	17 (14.9)	33 (11.4)	0.328†
No	351 (87)	96 (84.2)	255 (87.9)	
Unknown	3 (1)	1 (0.9)	2 (0.7)	
Comorbidities ≥	0	0	0	
2, n (%)	~		-	
Yes	303 (75)	92 (80.7)	211 (72.8)	0.087†

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Table	el.	Continued

Variable     Total     Non-COVID-19 (n = 114)     Non-COVID-19 (n = 290)     p-value       No     98 (24)     21 (18.4)     77 (26.6)     1       Unknown     3 (1)     1 (0.9)     2 (0.7)     5       Surgery, n(%)     V     2 (0.7)     0.073†       Hemiarthroplasty     13 (3.2)     4 (3.5)     9 (3.1)     0.073†       Hemiarthroplasty     160 (39.6)     46 (40.4)     114 (39.3)     0.73†       Hemiarthroplasty     121 (30.0)     26 (22.8)     95 (32.8)     16       DHS     121 (30.0)     26 (22.8)     95 (32.8)     16     14       Olmaniated screws     (15.2)     33 (28.9)     56 (19.3)     14       Conservative     10 (2.5)     5 (4.4)     5 (1.7)     14       Unknown     3 (0.7)     0 (0)     3 (1)     14       Spinal     160 (39.6)     41 (36)     19 (41)     14       N/A     15 (3.7)     5 (4.4)     10 (3.4)     14       N/A     16 (3.5)     5 (1.7)     14     14					
Variable     Total     (n = 114)     (n = 290)     p-value       No     98 (24)     21 (18.4)     77 (26.6)     10000     20.7)       Surgery, n (%)     2 (0.7)     20.7)     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     50000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     500000     5000000     5000000     5000000     5000000     5000000     5000000     5000000     5000000     5000000     5000000     5000000     5000000     5000000     50000000     50000000     50000000     500000000     500000000     500000000     5000000000000			COVID-19	Non-COVID-19	
No     98 (24)     21 (18.4)     77 (26.6)       Unknown     3 (1)     1 (0.9)     2 (0.7)       Surgery, n(%)     2     2 (0.7)       THA     13 (3.2)     4 (3.5)     9 (3.1)     0.073†       Hemiarthroplast     160 (39.6)     46 (40.4)     114 (39.3)     14       DHS     121 (30.0)     26 (22.8)     95 (32.8)     14       IM nail     91 (22.5)     33 (28.9)     56 (19.3)     14       Cannulated screws 6 (1.5)     0 (0)     6 (2.1)     14       Conservative     10 (2.5)     5 (4.4)     5 (1.7)     14       Unknown     3 (0.7)     0 (0)     3 (1)     14       Anaesthesia, n (%)     10 (2.5)     5 (4.4)     10 (3.4)       Spinal     160 (39.6)     41 (36)     19 (41)       N/A     15 (3.7)     5 (4.4)     10 (3.4)       Unknown     10 (2.5)     5 (4.4)     10 (3.4)       Unknown     10 (2.5)     5 (4.4)     1.45 (1.36)     0.756*       Surgery, days (SD)     Siter     Sit	Variable	Total	(n = 114)	(n = 290)	p-value
Unknown   3 (1)   1 (0.9)   2 (0.7)     Surgery, n(%)        THA   13 (3.2)   4 (3.5)   9 (3.1)   0.073 †     Hemiarthroplasty   160 (39.6)   46 (40.4)   114 (39.3)      DHS   121 (30.0)   26 (22.8)   95 (32.8)       IM nail   91 (22.5)   33 (28.9)   56 (19.3)       Cannulated screws (1.5)   0 (0)   6 (2.1)        Conservative   10 (2.5)   5 (4.4)   5 (1.7)        Maaesthesia, n (%)   3 (0.7)   0 (0)   3 (1)	No	98 (24)	21 (18.4)	77 (26.6)	
Surgery, n (%)   3 (3.2)   4 (3.5)   9 (3.1)   0.073 †     THA   16 (39.6)   46 (40.4)   114 (39.3)   D     DHS   121 (30.0)   26 (22.8)   95 (32.8)   I     IM nail   91 (22.5)   33 (28.9)   56 (19.3)   I     Cannulated screws 6 (1.5)   0 (0)   6 (2.1)   I     Conservative   10 (2.5)   5 (4.4)   5 (1.7)     Unknown   3 (0.7)   0 (0)   3 (1)     Anaesthesia, n (%)   IS (3.7)   63 (55.3)   156 (53.8)   0.376 †     Spinal   160 (39.6)   41 (36)   119 (41)   I     N/A   15 (3.7)   5 (4.4)   10 (3.4)   I     Unknown   10 (2.5)   5 (4.4)   10 (3.4)   I     N/A   15 (3.7)   5 (4.4)   1.45 (1.36)   0.756*     surgery, days   IS (3.7)   5 (4.4)   1.45 (1.36)   0.756*     Spinal   10 (2.5)   5 (4.4)   1.45 (1.36)   0.756*     Surgery, days   IS (3.7)   5 (4.4)   1.45 (1.36)   0.756*     Surgery, days   IS (3.	Unknown	3 (1)	1 (0.9)	2 (0.7)	
THA   13 (3.2)   4 (3.5)   9 (3.1)   0.073 [↑] Hemiarthroplasty   160 (39.6)   46 (40.4)   114 (39.3)      DHS   121 (30.0)   26 (22.8)   95 (32.8)      IM nail   91 (22.5)   33 (28.9)   56 (19.3)      Cannulated screws   6 (1.5)   0 (0)   6 (2.1)      Conservative   10 (2.5)   5 (4.4)   5 (1.7)      Unknown   3 (0.7)   0 (0)   3 (1)      Anaesthesia, n (%)   5 (1.7)        Spinal   160 (39.6)   41 (36)   119 (41)       N/A   15 (3.7)   5 (4.4)   10 (3.4)        Unknown   10 (2.5)   5 (4.4)   10 (3.4) <td>Surgery, n (%)</td> <td></td> <td></td> <td></td> <td></td>	Surgery, n (%)				
Hemiarthroplasty   160 (39.6)   46 (40.4)   114 (39.3)     DHS   121 (30.0)   26 (22.8)   95 (32.8)     IM nail   91 (22.5)   33 (28.9)   56 (19.3)     Cannulated screws   6 (1.5)   0 (0)   6 (2.1)     Conservative   10 (2.5)   5 (4.4)   5 (1.7)     Unknown   3 (0.7)   0 (0)   3 (1)     Anaesthesia, n (%)   K   K   K     GA   219 (54.2)   63 (55.3)   156 (53.8)   0.376 †     Spinal   160 (39.6)   41 (36)   119 (41)   146 (1.27)     N/A   15 (3.7)   5 (4.4)   10 (3.4)   146 (1.27)     Unknown   10 (2.5)   5 (4.4)   1.45 (1.36)   0.756*     surgery, days   K   K   K   K   K     (SD)   1.46 (1.27)   1.49 (1.01)   1.45 (1.36)   0.756*     surgery, days   K   K   K   K   K     (SD)   Time to surgery, days   K   K   K   K     <48 hrs	THA	13 (3.2)	4 (3.5)	9 (3.1)	0.073†
DHS   121 (30.0)   26 (22.8)   95 (32.8)     IM nail   91 (22.5)   33 (28.9)   56 (19.3)     Cannulated screws   6 (1.5)   6 (2.1)     Conservative   10 (2.5)   5 (4.4)   5 (1.7)     Unknown   3 (0.7)   0 (0)   3 (1)     Anaesthesia n (%)     GA   219 (54.2)   63 (55.3)   156 (53.8)   0.376†     Spinal   160 (39.6)   41 (36)   119 (41)   14     N/A   15 (3.7)   5 (4.4)   10 (3.4)   14     Unknown   10 (2.5)   5 (4.4)   5 (1.7)   145 (1.36)   0.756*     surgery, days   5 (3.7)   5 (4.4)   10 (3.4)   14   145 (1.56)   0.756*     Singery, days   5 (3.7)   5 (4.4)   1.45 (1.36)   0.756*   146 (1.27)   1.49 (1.01)   1.45 (1.36)   0.756*     Surgery, days   5   5   5   5   1.45 (1.36)   0.756*     surgery, days   5   7   6.61.4)   200 (69)   0.316†     < 48 hrs	Hemiarthroplasty	160 (39.6)	46 (40.4)	114 (39.3)	
IM nail   91 (22.5)   33 (28.9)   56 (19.3)     Cannulated screws   (1.5)   0 (0)   6 (2.1)     Conservative   10 (2.5)   5 (4.4)   5 (1.7)     Unknown   3 (0.7)   0 (0)   3 (1)     Anaesthesia, n (%)   5   5   5     GA   219 (54.2)   63 (55.3)   156 (53.8)   0.376 †     Spinal   160 (39.6)   41 (36)   119 (41)   1     N/A   15 (3.7)   5 (4.4)   10 (3.4)   1     Unknown   10 (2.5)   5 (4.4)   5 (1.7)   0.756 *     Surgery, days   S   S (1.27)   1.49 (1.01)   1.45 (1.36)   0.756 *     Surgery, days   S   S (1.27)   1.49 (1.01)   1.45 (1.36)   0.756 *     Surgery, days   S   S   S   S   S   S     Sime to surgery, days   270 (66.8)   70 (61.4)   200 (69)   0.316 †     < 48 hrs   118 (29.2)   38 (33.3)   80 (27.6)   S     Unknown/N/A   16 (4.0)   6 (5.3)   10 (3.4)   S	DHS	121 (30.0)	26 (22.8)	95 (32.8)	
Cannulated screws 6 (1.5)   0 (0)   6 (2.1)     Conservative   10 (2.5)   5 (4.4)   5 (1.7)     Unknown   3 (0.7)   0 (0)   3 (1)     Anaesthesia, n (%)   5 (3.7)   0 (0)   5 (53.8)   0.376†     GA   219 (54.2)   63 (55.3)   156 (53.8)   0.376†     Spinal   160 (39.6)   41 (36)   119 (41)   1     N/A   15 (3.7)   5 (4.4)   10 (3.4)   1     Unknown   10 (2.5)   5 (4.4)   5 (1.7)   1.45 (1.36)   0.756*     surgery, days   S   S   S   S   S   S     Shan time to (SD)   1.46 (1.27)   1.49 (1.01)   1.45 (1.36)   0.756*     surgery, days   S   S   S   S   S     (SD)   70 (66.8)   70 (61.4)   200 (69)   0.316†     ≤ 48 hrs   118 (29.2)   38 (33.3)   80 (27.6)   10 (3.4)	IM nail	91 (22.5)	33 (28.9)	56 (19.3)	
Conservative   10 (2.5)   5 (4.4)   5 (1.7)     Unknown   3 (0.7)   0 (0)   3 (1)     Anaesthesia, n	Cannulated screws	6 (1.5)	0 (0)	6 (2.1)	
Unknown   3 (0.7)   0 (0)   3 (1)     Anaesthesia, n	Conservative	10 (2.5)	5 (4.4)	5 (1.7)	
Anaesthesia, n   (%)     GA   219 (54.2)   63 (55.3)   156 (53.8)   0.376 †     Spinal   160 (39.6)   41 (36)   119 (41)     N/A   15 (3.7)   5 (4.4)   10 (3.4)     Unknown   10 (2.5)   5 (4.4)   5 (1.7)     Mean time to surgery, days   1.46 (1.27)   1.49 (1.01)   1.45 (1.36)   0.756*     Surgery, days	Unknown	3 (0.7)	0 (0)	3 (1)	
(%)     GA   219 (54.2)   63 (55.3)   156 (53.8)   0.376†     Spinal   160 (39.6)   41 (36)   119 (41)     N/A   15 (3.7)   5 (4.4)   10 (3.4)     Unknown   10 (2.5)   5 (4.4)   5 (1.7)     Mean time to surgery, days (SD)   1.46 (1.27)   1.49 (1.01)   1.45 (1.36)   0.756*     Time to surgery, r (%)   -   -   -   -   -     < 48 hrs	Anaesthesia, n				
GA   219 (54.2)   63 (55.3)   156 (53.8)   0.376†     Spinal   160 (39.6)   41 (36)   119 (41)     N/A   15 (3.7)   5 (4.4)   10 (3.4)     Unknown   10 (2.5)   5 (4.4)   5 (1.7)     Mean time to surgery, days (SD)   1.46 (1.27)   1.49 (1.01)   1.45 (1.36)   0.756*     Time to surgery, n (%)   270 (66.8)   70 (61.4)   200 (69)   0.316†     ≥ 48 hrs   118 (29.2)   38 (33.3)   80 (27.6)   Unknown/N/A	(%)				
Spinal   160 (39.6)   41 (36)   119 (41)     N/A   15 (3.7)   5 (4.4)   10 (3.4)     Unknown   10 (2.5)   5 (4.4)   5 (1.7)     Mean time to surgery, days (SD)   1.46 (1.27)   1.49 (1.01)   1.45 (1.36)   0.756*     Time to surgery, n (%)   270 (66.8)   70 (61.4)   200 (69)   0.316†     ≥ 48 hrs   118 (29.2)   38 (33.3)   80 (27.6)   Unknown/N/A   16 (4.0)   6 (5.3)   10 (3.4)	GA	219 (54.2)	63 (55.3)	156 (53.8)	0.376†
N/A     15 (3.7)     5 (4.4)     10 (3.4)       Unknown     10 (2.5)     5 (4.4)     5 (1.7)       Mean time to surgery, days (SD)     1.46 (1.27)     1.49 (1.01)     1.45 (1.36)     0.756*       Time to surgery, n (%)     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -     -	Spinal	160 (39.6)	41 (36)	119 (41)	
Unknown   10 (2.5)   5 (4.4)   5 (1.7)     Mean time to surgery, days   1.46 (1.27)   1.49 (1.01)   1.45 (1.36)   0.756*     Surgery, days	N/A	15 (3.7)	5 (4.4)	10 (3.4)	
Mean time to surgery, days (SD)     1.46 (1.27)     1.49 (1.01)     1.45 (1.36)     0.756*       Time to surgery, n (%)     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z <thz< th="">     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     <thz< th="">     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     Z     <thz< td=""><td>Unknown</td><td>10 (2.5)</td><td>5 (4.4)</td><td>5 (1.7)</td><td></td></thz<></thz<></thz<>	Unknown	10 (2.5)	5 (4.4)	5 (1.7)	
rime to surgery, n (%)   < 48 hrs	Mean time to surgery, days (SD)	1.46 (1.27)	1.49 (1.01)	1.45 (1.36)	0.756*
n (%) < 48 hrs 270 (66.8) 70 (61.4) 200 (69) 0.316† ≥ 48 hrs 118 (29.2) 38 (33.3) 80 (27.6) Unknown/N/A 16 (4.0) 6 (5.3) 10 (3.4)	Time to surgery,				
< 48 hrs 270 (66.8) 70 (61.4) 200 (69) 0.316† ≥ 48 hrs 118 (29.2) 38 (33.3) 80 (27.6) Unknown/N/A 16 (4.0) 6 (5.3) 10 (3.4)	n (%)				
≥ 48 hrs 118 (29.2) 38 (33.3) 80 (27.6) Unknown/N/A 16 (4.0) 6 (5.3) 10 (3.4)	< 48 hrs	270 (66.8)	70 (61.4)	200 (69)	0.316†
Unknown/N/A 16 (4.0) 6 (5.3) 10 (3.4)	≥ 48 hrs	118 (29.2)	38 (33.3)	80 (27.6)	
	Unknown/N/A	16 (4.0)	6 (5.3)	10 (3.4)	

*Mann-Whitney U test.

†Chi-squared test.

AMTS, Abbreviated Mental Test Score; ASA, American Society of Anesthesiologists Score; DHS, dynamic hip screw; GA, general anaesthesia; Hb, haemoglobin; IM, intramedullary; N/A, not applicable; NHFS, Nottingham Hip Fracture Score; NOF, neck of femur fracture; THA, total hip arthroplasty.

were positive COVID-19 diagnosis, male sex, and patients with  $\geq$  two co-morbidities (Table IV and Figure 2).

#### Discussion

Our study found that perioperative mortality was 14.4% (CI 11.07 to 17.73) across the whole cohort of patients. However, the risk of perioperative mortality was higher among those patients who had a positive test or high clinical suspicion for COVID-19. Furthermore, the overall perioperative mortality in our cohort is higher than data reported in the National Hip Fracture Database for England, Wales and Northern Ireland which reports an overall annualized 30-day mortality rate of 6.1%.³ Our data suggest an almost sixfold increased likelihood of mortality and an adjusted excess risk of 20% among hip fracture patients with a confirmed or suspected COVID-19 status when compared to those without a COVID-19 diagnosis. This also held true for male sex (OR 2.7, 95% CI 1.37 to 5.29) and patients with two or more comorbidities (OR 4.7, 95% CI 1.5 to 14.61) although with reduced odds ratios. Nevertheless, such findings ought to be interpreted with caution as the model of adjusting the analysis to factors that proved significant individually

Table II. Outcome measures.

Variable	Total	COVID-19 (n = 114)	Non-COVID-19 (n = 290)	p-value
Status at discharge, n (%)				
Alive	358 (88.6)	84 (73.7)	274 (94.5)	< 0.001*
Deceased	46 (11.4)	30 (26.3)	16 (5.5)	
Status at 30 days postoperative, n (%)				
Alive	346 (85.6)	77 (67.5)	269 (92.8)	< 0.001*
Deceased	58 (14.4)	37 (32.5)	21 (7.2)	
Discharge destination, n (%)				
Home	184 (46)	42 (22.8)	142 (77.2)	< 0.001*
Rehabilitation facility	71 (18)	17 (23.9)	54 (76.1)	
Residential care	33 (8)	6 (18.2)	27 (81.8)	
Nursing home	36 (9)	8 (22.2)	28 (77.8)	
Other hospital ward	17 (4)	3 (17.6)	14 (82.4)	
Inpatient	12 (3)	6 (50)	6 (50)	
Deceased at discharge	45 (11)	31 (68.9)	14 (31.1)	
Unknown	6 (1)	1 (16.7)	5 (83.3)	
Mean LOS, days (SD)	13.59 (8.81)	17.66 (11.16)	12.04 (7.17)	< 0.001†
Mean time to COVID-19 diagnosis, days (SD)	9.23 (8.06)	10.1 (7.69)	7.26 (8.58)	< 0.038†

*Chi-squared test

†Mann-Whitney U test.

LOS, length of stay.

**Table III.** Differences in mortality between the different methods ofCOVID-19 confirmation at 30 days postoperatively.

COVID-19 status, n (%)	Total	Alive (n = 346)	Deceased (n = 58)	p-value*
Positive by RT-PCR	109 (27.0)	75 (68.8)	34 (31.2)	0.015
Negative by RT-PCR	50 (12.4)	42 (84.0)	8 (16.0)	
Not tested	240 (59.4)	227 (94.6)	13 (5.4)	
Clinical signs and imaging	5 (1.2)	2 (40.0)	3 (60.0)	

*Fisher's exact test.

RT-PCR, reverse transcription polymerase chain reaction.

can conclude different results depending on which factors were analyzed, as shown in Supplementary Table iii, which demonstrates an example when combining COVID-19 status, age, sex, TTS, ASA and NHFS, male sex no longer held the same statistical significance. Reassuringly, irrespective of the differing covariates analyzed, positive COVID-19 status holds its clinically and statistically significant impact on mortality.

The exact cause of death was not collected and hence is a limitation of our study's findings. There was heterogeneity in the way data was obtained with some centres reporting COVID-19 as a cause of death while others did not. Hence we could not group the patients nor could we seek further clarification through official death certificate reports during the early phase of the COVID-19 pandemic when the healthcare system was under significant strain. Furthermore the effects on allied services such as those provided by orthogeriatric colleagues, whose involvement in the care of hip fracture patients has proven to reduce mortality, was not determined within this study and is a further limitation.¹³ The COVIDSURG international collaborative group reported a 23.8% 30-day mortality rate among 1,128 surgical patients with perioperative COVID-19 infection between 1 January 2020 and 31 March 2020. It is of note that of the 302 orthopaedic patients, 262 were emergency. At least 115 were hip fracture patients (likely more) and though no sub-group analysis was reported, these rates of mortality are certainly similar to those observed in this study and others in significantly affected countries.^{5-9,14}

Overall, 40% (159/404) of the included patients underwent COVID-19 testing by RT-PCR, with 96% (109/114) of the cases confirmed this way. Unfortunately, with our study occurring during the early stages of the pandemic and as per Public Health England guidance, routine laboratory testing across the included centres was not carried out on all patients but instead was limited to only those who experienced symptoms suggestive of the COVID-19 infection. Hence, routine invasive testing of all patients regardless of clinical status would have required further ethical approval. Additionally it would have further strained the healthcare system's testing capacity which was already under considerable pressure. Routine testing of all emergency patients admitted to NHS hospitals only came in to force on the 27 April 2020.

A small number of patients (5/114, 1.2%) were included within our COVID-19 cohort as their clinical picture and imaging strongly favoured such a diagnosis. Given that COVID-19 diagnosis can be accurately made by appropriate imaging, we felt it valid to include such patients within our analysis.¹⁵ Conversely, 12.4% (50/114) of the patients proved negative by RT-PCR. The moderate

		Unadjusted analysis		Adjusted analysis (R ² 0.312)	
Characteristics	n (% deceased)	OR (95% CI)	p-value	OR (95% CI)	p-value
COVID-19 status					
COVID-19 cohort	114 (32.5)	6.15 (3.40 to 11.13)	< 0.001	5.64 (2.95 to 10.80)	< 0.001
Non COVID-19 cohort*	290 (7.2)	N/A	N/A	N/A	N/A
Age					
Mean	N/A	1.05 (1.01 to 1.08)	0.015	N/A	N/A
Age < 85 yrs*	194 (9.8)	N/A	N/A	N/A	N/A
Age ≥ 85 yrs	210 (18.6)	2.10 (1.17 to 3.78)	0.013	1.72 (0.87 to 3.41)	0.120
Sex					
Male	123 (22.8)	2.47 (1.40 to 4.35)	0.002	2.69 (1.37 to 5.29)	0.004
Female*	281 (10.7)	N/A	N/A	N/A	N/A
Time to surgery					
Mean	N/A	1.32 (1.09 to 1.59)	0.004	N/A	N/A
< 48 hrs*	270 (12.2)	N/A	N/A	N/A	N/A
≥ 48 hrs	118 (16.9)	1.47 (0.80 to 2.68)	0.214	1.20 (0.60 to 2.41)	0.606
Unknown/ N/A	16 (8.6)	3.26 (1.07 to 9.99)	0.038	4.12 (0.94 to 18.05)	0.600
Pre-admission residence					
Home*	309 (11.7)	N/A	N/A	N/A	N/A
Institutional care	89 (22.5)	2.20 (1.20 to 4.03)	0.011	1.44 (0.64 to 3.28)	0.377
Unknown	6 (33.3)	3.79 (0.67 to 21.44)	0.132	1.16 (0.09 to 14.32)	0.911
AMTS					
Mean	N/A	0.87 (0.80 to 0.94)	< 0.001	N/A	N/A
AMTS ≥ 7*	253 (10.3)	N/A	N/A	N/A	N/A
AMTS ≤ 6	128 (21.1)	2.33 (1.30 to 4.20)	0.005	2.13 (0.99 to 4.62)	0.540
Unknown	23 (21.7)	2.43 (0.83 to 7.08)	0.105	1.64 (0.42 to 6.40)	0.479
ASA score					
Mean	N/A	1.95 (1.26 to 3.02)	0.003	N/A	N/A
ASA 1 and 2*	58 (12.1)	N/A	N/A	N/A	N/A
ASA 3+	336 (15.2)	1.30 (0.56 to 3.03)	0.538	0.30 (0.09 to 1.02)	0.055
Unknown	10 (0)	Not estimable	0.999	Not estimable	0.999
NHFS					
Mean	N/A	1.68 (1.34 to 2.09)	< 0.001	N/A	N/A
NHFS ≤ 5*	219 (9.1)	2.57 (1.44 to 4.60)	0.001	N/A	N/A
NHFS ≥ 6	185 (20.5)	N/A	N/A	N/A	N/A
Malignancy					
Yes	52 (11.5)	0.69 (0.08 to 6.29)	0.741	N/A	N/A
No*	347 (14.7)	N/A	N/A	N/A	N/A
Unknown	5 (20)	0.59 (0.05 to 5.47)	0.588	N/A	N/A
Pre-admission Hb					
< 10	50 (24)	2.15 (1.05 to 4.41)	0.038	1.87 (0.80 to 4.41)	0.151
≥ 10*	351 (14.8)	N/A	N/A	N/A	N/A
Unknown	3 (33)	3.4 (0.30 to 38.26)	0.322	6.13 (0.09 to 410.60)	N/A
Comorbidities					
< 2*	303 (5.1)	N/A	N/A	N/A	N/A
≥ 2	98 (17.2)	3.85 (1.49 to 9.94)	0.005	4.68 (1.50 to 14.61)	0.008
Unknown	3 (50)	9 3 (0 72 to 120 73)	0.088	N/A	N/A

Table IV. Unadjusted and adjusted sensitivity analysis of predictors of 30 day postoperative mortality.

*Reference.

AMTS, Abbreviated Mental Test Score; ASA, American Society of Anesthesiologists Score; CI, confidence interval; NHFS, Nottingham Hip Fracture Score; OR, odds ratio.

sensitivity of this test to provide false negative results of 2% to 29% and with our data showing that the positive cohort had a 30-day postoperative mortality of 31.2%, and negative cohort 16%, it is possible that some of the confirmed negative patients were indeed positive and hence misplaced for final analysis.^{16,17} This is especially

notable as the "not tested" cohort demonstrated a mortality rate of 5.4%, which is similar to that observed prior to the pandemic.³

Differences in length of hospital stay between the two cohorts were also observed, with the COVID-19 cohort group having a longer stay by a mean of 5.5 days. While



Adjusted analysis for predictors of 30 day postoperative mortality. AMTS, Abbreviated Mental Test Score, ASA, American Society of Anesthesiologists grade, Hb,haemoglobin, TTS, time to surgery.

our study was not designed to discern the true reason behind this, it would not be unfair to assume that the positive group were significantly sicker, requiring greater input, effort and time for their care and recovery. Relatedly, with the non-COVID-19 cohort technically being asymptomatic and hence assumed safer for discharge and with hospitals under pressure to retain appropriate capacity for the anticipated COVID-19 peak in early April 2020, it is possible that some of the observed length of hospital stay disparity could be construed to this. Reiterating the falsenegative issue with testing, a proportion of otherwise COVID-19 positive patients might have been discharged to institutional care given that the non-COVID-19 group (55/69; 80%) accounted for a large proportion of these. Equally, COVID-19 doesn't always lead to a clinical manifestation with up to 40% of patients remaining asymptomatic throughout the duration of COVID-19 infection.^{18,19} From 15 April 2020 it became mandatory for all patients being discharged to care institutions to undergo routine testing prior to discharge from hospital.²⁰

With regard to patients who underwent COVID-19 testing, we found that the majority of testing and subsequent confirmation of a positive result occurred in the postoperative period (mean 9.23 days after surgery (SD 8.06). One could hypothesize that their infection was perhaps secondary to nosocomial spread. However, given the incubation period of COVID-19 (which ranges from 2 to 14 days), such conjecture would be incorrect. It is just as likely that these patients acquired the infection in the community prior to admission.²¹

We are also aware that there has been a wide regional variation of COVID-19 prevalence and hence our findings must be applied cautiously across the whole of the UK. The West Midlands, which is one of the most populous regions in the UK with 5.9 million inhabitants, was particularly hard hit.²² At the time of undertaking this work, it was the second-worst hit region with COVID-19 disease behind London (43.2 deaths per 100,000).²³ Interestingly, there were no observed deaths in the other centre from the northwest of England. Conversely, the two

UK-based published studies have reported differences in COVID-19 prevalence among their cohorts with the Scottish team recording a prevalence of 9% while the team from London reported 18%, which are considerably different to our figure of 28%.^{8,9}

The testing strategy in the UK has changed significantly since the undertaking of this study; however, the prevalence of the disease has also evolved. Therefore, though future studies within the UK may provide us with a more accurate reflection of disease prevalence, this will be at a very different stage of the pandemic. Serological antibody testing has now also been introduced and in time this may give us a clearer idea of previous infection rates and regional variability. Additionally, this study was undertaken during the peak of the pandemic in England (R number = 4) and therefore does not reflect the current situation where rates of new infection and mortality have fallen considerably. Nevertheless, COVID-19 prevalence is ever evolving given the developments of September 2020 reporting an increase in the R number from < 1 toward 1.5, hence the findings reported here and elsewhere maintain their importance and relevance.24

The limitations of this study have been alluded to above in terms of data collection, testing variability, sensitivity and geographical differences in COVID-19 prevalence. These were unfortunately unavoidable, with testing variability being a product of Public Health England policy.

Although our sample size may be deemed small given the wide confidence intervals this is nevertheless one of the largest studies looking at the impact of COVID-19 on hip fracture patients worldwide, containing more or an equivalent number of patients to the published studies to date.⁵⁻⁹ Additionally, the presence of the non-COVID-19 comparator allows differences among the two groups to be highlighted unlike the COVIDSURG Collaborative who reviewed only COVID-19 surgical cases.¹⁴

The findings from this study clearly demonstrate the significant additional risk to hip fracture patients who develop COVID-19 infection within 30 days of surgery (or admission if managed nonoperatively). It also highlights factors associated with acquiring COVID-19 infection, although the results may not present a new or surprising finding given the detrimental effect COVID-19 has had on the world's population. We nevertheless feel that this piece of work is important, as it allows us to counsel patients and their families of the potential risks of being admitted with a hip fracture during a period when hospitals are placed under pressure from highly infectious diseases.

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#### **Supplementary material**

Tables displaying regional distribution of patients, adjusted excess mortality risk analysis, and unadjusted and adjusted sensitivity analysis of predic-

tors of 30-day postoperative mortality.

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- I. Ahmed: Collected local data, Wrote the manuscript.
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- P. K. Kimani: Performed the statistical analysis, Wrote the manuscript. P. Wall: Wrote the manuscript, Oversaw the final document.
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#### Ethical review statement:

The study was registered with the research and audit department of each participating UK centre.

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