JB&JS OPEN ACCESS

Mortality in Patients with Proximal Femoral Fracture During the COVID-19 Pandemic

A U.K. Hospital's Experience

Georgios Mamarelis, MD, MRCSEd, Uche Oduoza, MBBS, MSc, MRCSEng, Ravi Chekuri, MBBS, MS, MRCSEng, Rami Estfan, MD, MRCSEd, and Tony Greer, MBChB, FRCS

Investigation performed at the Department of Orthopaedics, Southend University Hospital, Essex, United Kingdom

Background: Coronavirus disease 2019 (COVID-19) is a worldwide pandemic, with a case mortality ratio of approximately 6.4% at the time of writing (May 2020). Mortality increases in elderly patients with comorbidities. Patients with hip fracture have an average age of 80 years, with an estimated 2.8 comorbidities per patient. Evidence is lacking regarding the mortality rate of patients with hip fracture admitted during the COVID-19 pandemic. Our aim was to investigate the mortality rate among patients with a proximal femoral fracture who were admitted to our hospital during the COVID-19 pandemic.

Methods: We conducted a retrospective review of all patients with a proximal femoral fracture admitted to Southend University Hospital in the U.K. from March to April 2020 (during the COVID-19 pandemic). Data collected included demographics (patient age, body mass index, sex), comorbidities, and blood test values along with COVID-19 diagnosis (based on positive microbiological sample and clinical and radiographic findings) and operative characteristics (time to operation, length of stay, American Society of Anesthesiologists [ASA] classification, Nottingham Hip Fracture Score). The primary outcome was the 30-day mortality rate for patients with a hip fracture who were COVID-19 positive or negative. Kaplan-Meier survival analysis was conducted along with Mann-Whitney U tests and Fisher exact tests.

Results: Forty-one patients were included in the study, of whom 37 had an available SARS-CoV-2 (severe acute respiratory syndrome-coronavirus 2) swab test result. The overall 30-day mortality was 22%. Eleven patients tested positive for COVID-19. There was a significant difference in the mortality rate between those who tested positive and those who tested negative (54.5% versus 7.69%, respectively; Fisher exact test, $p = 0.004$) and between the operative patients who tested positive and the operative patients who tested negative (37.5% versus 4.34%, respectively; Fisher exact test, $p = 0.043$).

Conclusions: Patients with a proximal femoral fracture may be at higher risk for mortality during the COVID-19 pandemic. We noted that patients with a proximal femoral fracture who tested positive for COVID-19 had a higher 30-day mortality rate compared with those who tested negative. Additional research is required to ascertain the benefits of a reduction in time to operation.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

The outbreak of coronavirus disease 2019 (COVID-19), caused by the novel coronavirus SARS-CoV-2 (severe acute respiratory syndrome-coronavirus 2), has evolved into a worldwide pandemic, with >5 million confirmed cases and a case mortality ratio of approximately 6.4% at the time of manuscript preparation (May 2020)[1,2]. As of mid-October 2020, >38 million cases had been confirmed globally[1].

The U.K. has been one of the most severely affected countries[3]. At the time of writing (May 22, 2020), there were 36,393 deaths registered in England and Wales involving COVID-19[4]. The pandemic has caused unprecedented pressure on the National Health Service in the U.K., leading to changes in trauma service provided by hospitals. British Orthopaedic Association guidance during this period stated that hip fractures required

Disclosure: The authors indicated that no external funding was received for any aspect of this work. The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJSOA/A222).

"obligatory surgery" and would continue to require hospital admission[5].

In our center, elderly patients with hip fractures have continued to receive operative treatment throughout the pandemic, despite increasing concerns surrounding susceptibility to COVID-19. Prior to SARS-CoV-2, patients in the U.K. with a hip fracture had a 30-day mortality rate of between 8% to 10%[6,7]. There is little evidence regarding mortality rates and outcomes in patients with hip fractures with concurrent COVID-19. One study from Spain reported a mean 14-day mortality rate of 30.4% for these patients[8].

Patients >65 years of age and those with multiple comorbidities are known to have a higher mortality rate with COVID-19[9,10]. The majority of deaths in the U.K. associated with COVID-19 (33,098 of 36,393) have been among people aged ≥65 years, with 46% (15,079) of these occurring in the age group of >85 years[11]. The average age for a patient with a hip fracture is 80 years, with an estimated 2.8 comorbidities per patient reported in the literature[12]. Given these facts, patients with hip fracture are a particularly vulnerable group, and more information is required regarding the effect on mortality rate of COVID-19 among patients with a concurrent hip fracture.

Our primary aims were to evaluate the 30-day mortality rate for patients with a proximal femoral fracture during the COVID-19 pandemic and to compare the mortality rates between patients with such fractures who were positive or negative for COVID-19.

Materials and Methods

This was a retrospective study of all hip fractures (proximal femoral fractures) at Southend University Hospital, Southend-on-Sea, U.K., from March to April 2020. Patients details were collected from a prospective database of all patients with proximal femoral fractures admitted to the hospital.

In all, 41 patients with a proximal femoral fracture on admission (27 female, 14 male; mean age, 80.34 years [range, 47 to 99 years]) were included (Table I). Twenty-six (63.4%) of the patients had a nerve block in the emergency department. Thirty-five patients (mean age, 80.06 years [range, 47 to 99 years]) underwent surgery. For 6 patients (mean age, 82.00 years [range, 65 to 92 years]), surgery was cancelled; 5 of the 6 patients were medically unwell because of COVID-19 infection, and the remaining patient was treated with nonoperative management. There were 31 patients in the surgical group of 35 with a confirmed COVID-19 status (positive or negative).

Surgery was performed or supervised by a senior orthopaedic surgeon. The implant used was chosen by the responsible senior surgeon. The same implants were used for each type of procedure.

Data collected for each patient consisted of sex, date of birth, body mass index (BMI), American Society of Anesthesiologists (ASA) grade and comorbidities[13], admission date and time, residence status pre- and post-hospital admission, operative treatment details, length of stay, complications and readmission details, radiography and computed tomography (CT) scan reports regarding COVID-19, and results of SARS-CoV-2 RNA real-time reverse transcription polymerase chain reaction (RT-PCR) swab testing. Date of death was collected from our local registry of deaths, which includes any patient who died as an inpatient or in the community. Furthermore, we collected the causes of death from postmortem certificates in the hospital. Relevant laboratory tests were obtained for patients on admission, such as hemoglobin (Hb) level, white blood-cell (WBC) and lymphocyte counts, alanine aminotransferase (ALT) level, and C-reactive protein (CRP) level.

TABLE I Type of Fracture*

	No. of Patients	%
Fracture type		
Intracapsular displaced (31B1/31B2/31B3)	20	48.8
Intracapsular nondisplaced (31B1)	5	12.2
Extracapsular (31A1/31A2)	7	17.1
Extracapsular (31A3) (including reverse oblique)	6	14.6
Subtrochanteric (32A/32B/32C)	3	7.3
Total	41	100.0

*Fracture classification per the OTA/AO classification system[23].

We defined a diagnosis of COVID-19 as positive microbiological samples (RT-PCR swab) at any time during the admission. We also took into consideration clinical signs (cough, dyspnea) or positive radiographic findings (radiograph or chest CT scan). We performed swab tests for all patients admitted to the hospital; for 4 patients, swab data were not available (invalid/lost), leaving 37 patients with COVID-19 test results. Comparisons were made between patients with a proximal femoral fracture who were confirmed as COVID-19 positive and COVID-19 negative.

The primary outcome measure was 30-day mortality rate.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics (version 24) and Stata/MP (version 14.0; Stata Corp). A p value of <0.05 was considered significant. A Kolmogorov-Smirnov test was used to assess the normality of continuous data. Subsequently, a t test was used for parametric data, whereas a Mann-Whitney U test was used for nonparametric data. A Fisher exact test or chi-square test was used to compare proportions; the Altman arithmetic calculation was used for the relative risk (RR) with 95% confidence interval (CI)[14]. Confirmed positive COVID-19 status relative to mortality was assessed using Kaplan-Meier survival analysis with 95% CIs.

Results

Of the 41 patients who presented with hip fracture, 37 had an available COVID-19 test result; 11 patients tested positive and 26, negative. Thirty-five of the 41 patients received operative treatment. Of these, COVID-19 status was known for 31; 8 patients tested positive and 23, negative. Patient sex, age at

JBJS Open Access • 2020:e20.00086. **openaccess.jbjs.org** 3

TABLE II Comparison of Patients Treated Surgically for Proximal Femoral Fracture by COVID-19 Status (Positive or Negative)

	Operative Patients		
	COVID-Positive (N = 8)	COVID-Negative (N = 23)	P Value
Age* *(yr)*	83.63 ± 10.21	78.09 ± 10.25	0.198 (t = 1.317)
Female sex *(no. [%])*	5 (62.5%)	16 (69.6%)	0.712 (χ^2 = 0.136)
Operative side: right *(no. [%])*	5 (62.5.%)	13 (56.5%)	0.768 (χ^2 = 0.087)
Time from admission to operation* *(hr)*	36.8 ± 16.08	32.9 ± 21.62	0.386 (Mann-Whitney U = 72.000)
ASA classification *(no.)*			0.173 (χ^2 = 3.505)
1	0	0	
2	2	2	
3	3	17	
4	3	4	

*The values are given as the mean and standard deviation.

the time of surgery, operative side, time from admission to operation, and ASA grade were comparable between those who were COVID-19 positive and those who were negative (Table II).

Patients with COVID-19

As stated above, 11 of the total of 37 patients with a COVID-19 test had a positive result. Nine of the 11 patients had a positive test on the day of admission. One of the remaining 2 patients who had initially tested negative on admission developed respiratory symptoms 2 days postoperatively and subsequently had a second swab test 7 days post-admission, with a positive result. The final patient died 7 days after admission and tested positive postmortem.

Among the 11 patients who tested positive for COVID-19, 8 received operative treatment and 3 received nonoperative treatment for their proximal femoral fracture. Five of the 8 operative patients were symptomatic for COVID-19, with a high WBC count, a high CRP level, a low oxygen-saturation level, and/or a cough and fever, which they developed within 12 to 24 hours of admission. Three of the 8 operative patients remained asymptomatic during their admission. All 3 of the nonoperative patients were symptomatic, with a low oxygen-saturation level, a high WBC count, a high CRP level, and a low lymphocyte count. Two of the patients had a high temperature (>37.8°C), while the third patient presented with hypothermia (32°C). They were all considered critically ill patients following anesthetic review.

30-Day Mortality

The combined overall 30-day mortality rate was 22% (9 of 41 patients). We separated our sample into 2 major groups to assess the mortality rate in relation to COVID-19 status. The first group included any patient with a proximal femoral fracture (with or without operative treatment) who had a COVID-19 test at any time during their admission (37 patients). In this group, the overall 30-day mortality rate was 21.6% (8 patients) and predicted mortality on the basis of the Nottingham Hip Fracture Score (NHFS) was a mean (and standard deviation) of 11.22% ± 6.12% (range, 1.5% to 23%; 95% CI, 9.18% to 13.27%). There was a significant difference in the 30-day mortality rate between patients who were COVID-19 positive (54.5%) and those who were COVID-19 negative (7.69%) (Fisher exact test, p = 0.004). Kaplan-Meier analysis demonstrated a difference in mortality associated with positive or negative COVID status and concurrent hip fracture (log-rank test, p = 0.003) (Fig. 1).

The second group included any patient treated operatively for a proximal femoral fracture who had a COVID-19 test at any time during their admission (31 patients). The 30-day mortality rate was 12.9% (4 patients), and the NHFS predicted mortality was a mean of 10.4% ± 5.77% (range, 1.5% to 23%; 95% CI, 8.31% to 12.54%). In this group of operative patients, there was a significant difference in the 30-day mortality rate between those who were COVID-19 positive and those who

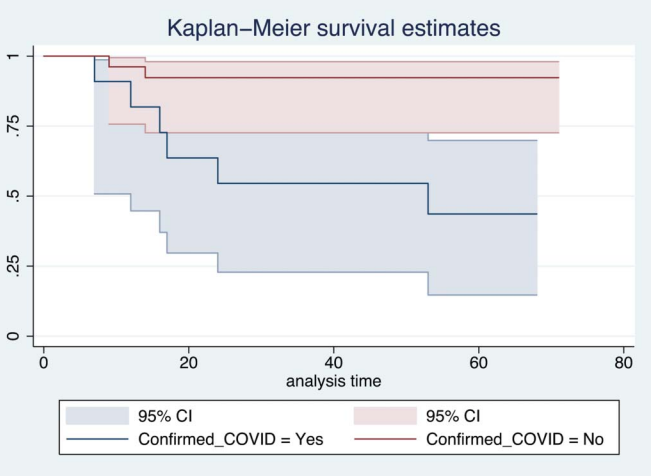

Fig. 1

Kaplan-Meier survival estimates (with 95% CI) for patients with a hip fracture, with or without operative treatment, by COVID-19 test result (positive or negative). Time is given in days.

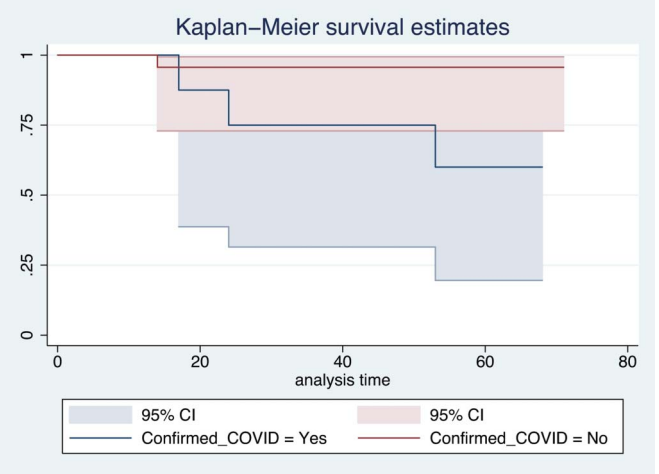

Fig. 2

Kaplan-Meier survival estimates (with 95% CI) for patients treated operatively for a hip fracture, by COVID-19 test result (positive or negative). Time is given in days.

were COVID-19 negative (37.5% versus 4.34% respectively; Fisher exact test, $p = 0.043$). Overall in this group, Kaplan-Meier analysis demonstrated a significant difference between patients who tested positive and those who tested negative for COVID-19 with regard to the mortality rate over the 30-day interval (log-rank test, $p < 0.04$). (Fig. 2).

Of the 6 patients who had their operation cancelled, 4 died (66.7% mortality). Three of these patients were confirmed to be COVID-19 positive, and the other 3 had a negative swab result. There was no significance in 30-day mortality between the COVID-19 positive and negative patients (Fisher exact test, $p > 0.05$).

Discussion

In this retrospective observational study, we investigated the mortality rate for patients with a proximal femoral fracture who were admitted to Southend University Hospital, U.K. Our primary aim was to calculate and report any increase in mortality associated with COVID-19 in this particularly vulnerable patient group. The overall 30-day mortality of patients within the study group was 21.95%, which is double the reported overall mortality rate in a similar Spanish study[8]. This is also approximately 3 times the 30-day mortality reported at the same center in March 2019 (7.5%)[15]. In the U.K., the national average 30-day mortality associated with proximal femoral fractures was 6.2% (February 2020)[15], with Southend slightly below the national average, at 5.2% (February 2020). The rise to 21.95% for all patients admitted over the study period is a considerable increase, which leads us to believe there is an association between SARS-CoV-2 and mortality in this particular group of patients.

Those in the study who tested positive for SARS-CoV-2 had a mortality rate of 54.5% compared with 7.69% for those who had a negative test result; the difference in mortality was significant ($p = 0.004$). These results varied from a similar study in Spain in which 14-day mortality rate for patients with a fractured femoral neck was 30.4% for those who tested positive for COVID-19 and was 10.3% for those testing negative[8]. Differences could be attributed to the lower 30-day mortality rate reported in Spain prior to the pandemic. In the 31 patients in the current study who were tested for COVID-19 and underwent surgery for a proximal femoral fracture, there was an observed higher rate of mortality for those who tested positive compared with those who tested negative.

Public Health England and the Johns Hopkins dashboard both calculated the case fatality ratio of COVID-19 patients in the U.K. as 14.3% as of May 22, 2020 (254,195 cases and 36,393 deaths) across all age groups in the U.K.[1,4]. Several studies have shown that mortality risk increases with age[16-18]. In our study, the mean age was 80 years (range, 47 to 99 years) with a substantial percentage of patients >65 years of age. This may account for the increased observed mortality reported in our study group. The increase in mortality with age was not replicated in our study. This may be in part due to our study being underpowered to detect a difference.

The observed mortality in our study also varied from the predicted 30-day mortality calculated using the NHFS[19,20]. The 11% predicted 30-day mortality for our study group was an underestimate compared with the observed result (22% mortality). This would add further credence to the observation that COVID-19 increases mortality.

Nonoperative management of proximal femoral fractures was found in a previous study to be associated with increased mortality compared with operative treatment over 1 year[21]. This was also true in our study; there was a 30-day mortality rate of 66.7% for patients treated without surgery. The mortality rate was elevated compared with pre-COVID-19 literature[22]. Given such findings, there may be a limited role for nonoperative treatment for proximal femoral fractures during the COVID-19 pandemic. Such findings would need to be corroborated in a large sample size.

Limitations

While we have reported a significantly higher 30-day mortality rate in patients with proximal femoral fracture who tested positive for COVID-19 compared with those who tested negative, the ability to draw conclusions from this is limited due to the nature of the study. The relatively small sample size may be underpowered to identify valid associations. In addition, we have 30-day mortality data but no long-term data as of yet. In spite of this, we believe that our study population is generalizable to that of the U.K., as key demographics such as age and comorbidities are similar to national averages.

Future Research

We believe that prospective studies assessing the risk factors leading to higher rates of mortality should be investigated to enable potential preventive strategies and risk mitigation.

Conclusions

On the basis of our findings, patients with proximal femoral fracture may be at higher risk for mortality during the COVID-19 pandemic. Among patients with proximal femoral fracture who tested positive for COVID-19, we noted a higher 30-day mortality rate than that seen for those who tested negative. Additional

research is required to ascertain the benefits of a reduction in time to operation as well as potential prevention strategies to protect elderly patients at risk of hip fracture.

This study enables us to further understand the effects of COVID-19 on patients with a proximal femoral fracture and alert health-care professionals and patients to the elevated 30-day mortality rate that we found among patients with a proximal femoral fracture who tested positive for COVID-19. ■

Georgios Mamarelis, MD, MRCSEd[1]
Uche Oduoza, MBBS, MSc, MRCSEng[1]
Ravi Chekuri, MBBS, MS, MRCSEng[1]
Rami Estfan, MD, MRCSEd[1]
Tony Greer, MBChB, FRCS[1]

[1]Department of Orthopaedics, Southend University Hospital, Essex, United Kingdom

Email address for G. Mamarelis: george.mamarelis@hotmail.com
Email address for U. Oduoza: u.oduoza@nhs.net
Email address for R. Chekuri: r.chekuri@nhs.net
Email address for R. Estfan: rami.estfan@southend.nhs.uk
Email address for T. Greer: tony.greer@southend.nhs.uk

ORCID iD for G. Mamarelis: 0000-0002-9241-3907
ORCID iD for U. Oduoza: 0000-0001-8651-3090
ORCID iD for R. Chekuri: 0000-0001-9055-969X
ORCID iD for R. Estfan: 0000-0002-7146-8781
ORCID iD for T. Greer: 0000-0002-8393-919X

References

1. Johns Hopkins University. COVID-19 dashboard by the Center for Systems Science and Engineering at John Hopkins University. Coronavirus Resource Center. 2020. Accessed 2020 Oct 15. https://coronavirus.jhu.edu/

2. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020 Feb 20;382(8):727-33. Epub 2020 Jan 24.

3. Jit M, Jombart T, Nightingale ES, Endo A, Abbott S, Edmunds WJ; LSHTM Centre for Mathematical Modelling of Infectious Diseases COVID-19 Working Group. Estimating number of cases and spread of coronavirus disease (COVID-19) using critical care admissions, United Kingdom, February to March 2020. Euro Surveill. 2020 May;25(18).

4. Gov.uk. Coronavirus cases in the UK: daily updated statistics. 2020. Accessed 2020 Sep 30. https://www.gov.uk/guidance/coronavirus-covid-19-information-for-the-public

5. British OA. Management of patients with urgent orthopaedic conditions and trauma during the coronavirus pandemic. 2020 Apr. Accessed 2020 Oct 19. https://www.boa.ac.uk/uploads/assets/ee39d8a8-9457-4533-9774e973c835246d/4e3170c2-d85f-4162-a32500f54b1e3b1f/COVID-19-BOASTs-Combined-FINAL.pdf

6. Giannoulis D, Calori GM, Giannoudis PV. Thirty-day mortality after hip fractures: has anything changed? Eur J Orthop Surg Traumatol. 2016 May;26(4):365-70. Epub 2016 Mar 4.

7. Neuburger J, Currie C, Wakeman R, Tsang C, Plant F, De Stavola B, Cromwell DA, van der Meulen J. The impact of a national clinician-led audit initiative on care and mortality after hip fracture in England: an external evaluation using time trends in non-audit data. Med Care. 2015 Aug;53(8):686-91.

8. Muñoz Vives JM, Jornet-Gibert M, Cámara-Cabrera J, Esteban PL, Brunet L, Delgado-Flores L, Camacho-Carrasco P, Torner P, Marcano-Fernández F; Spanish HIP-COVID Investigation Group. Mortality rates of patients with proximal femoral fracture in a worldwide pandemic: preliminary results of the Spanish HIP-COVID observational study. J Bone Joint Surg Am. 2020 Jul 1;102(13):e69.

9. Wang X, Fang X, Cai Z, Wu X, Gao X, Min J, Wang F. Comorbid chronic diseases and acute organ injuries are strongly correlated with disease severity and mortality among COVID-19 patients: a systemic review and meta-analysis. Research (Wash D C). 2020 Apr 19;2020:2402961.

10. Banerjee A, Pasea L, Harris S, Gonzalez-Izquierdo A, Torralbo A, Shallcross L, Noursadeghi M, Pillay D, Sebire N, Holmes C, Pagel C, Wong WK, Langenberg C, Williams B, Denaxas S, Hemingway H. Estimating excess 1-year mortality associated with the COVID-19 pandemic according to underlying conditions and age: a population-based cohort study. Lancet. 2020 May 30;395(10238):1715-25. Epub 2020 May 12.

11. Office for National Statistics. Deaths registered weekly in England and Wales, provisional: week ending 8 May 2020. 2020. Accessed 2020 Sep 30. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/weeklyprovisionalfiguresondeathsregisteredinenglandandwales

12. Lloyd R, Baker G, MacDonald J, Thompson NW. Co-morbidities in patients with a hip fracture. Ulster Med J. 2019 Sep;88(3):162-6. Epub 2019 Oct 11.

13. Dripps RD, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. JAMA. 1961 Oct 21;178:261-6.

14. Altman D. Practical statistics for medical research. New York: Chapman and Hall/CRC; 1990.

15. Royal College of Physicians. National Hip Fracture Database. Falls and Fragility Fracture Audit Programme. 2019. Accessed 2020 Sep 30. https://www.rcplondon.ac.uk/projects/falls-and-fragility-fracture-audit-programme-fffap#:~:text=The%20Falls%20and%20Fragility%20Fracture,to%20facilitate%20quality%20improvement%20initiatives

16. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar 28;395(10229):1054-62. Epub 2020 Mar 11.

17. Du RH, Liang LR, Yang CQ, Wang W, Cao TZ, Li M, Guo GY, Du J, Zheng CL, Zhu Q, Hu M, Li XY, Peng P, Shi HZ. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. Eur Respir J. 2020 May 7;55(5):2000524.

18. Leung C. Risk factors for predicting mortality in elderly patients with COVID-19: a review of clinical data in China. Mech Ageing Dev. 2020 Jun;188:111255. Epub 2020 Apr 27.

19. Wiles MD, Moran CG, Sahota O, Moppett IK. Nottingham Hip Fracture Score as a predictor of one year mortality in patients undergoing surgical repair of fractured neck of femur. Br J Anaesth. 2011 Apr;106(4):501-4. Epub 2011 Jan 28.

20. Moppett IK, Parker M, Griffiths R, Bowers T, White SM, Moran CG. Nottingham Hip Fracture Score: longitudinal and multi-assessment. Br J Anaesth. 2012 Oct;109(4):546-50. Epub 2012 Jun 22.

21. Frenkel Rutenberg T, Assaly A, Vitenberg M, Shemesh S, Burg A, Haviv B, Velkes S. Outcome of non-surgical treatment of proximal femur fractures in the fragile elderly population. Injury. 2019 Jul;50(7):1347-52. Epub 2019 May 22.

22. Hossain M, Neelapala V, Andrew JG. Results of non-operative treatment following hip fracture compared to surgical intervention. Injury. 2009 Apr;40(4):418-21. Epub 2009 Feb 23.

23. Meinberg EG, Agel J, Roberts CS, Karam MD, Kellam JF. Introduction: fracture and dislocation classification compendium-2018. J Orthop Trauma. 2018 Jan;32(Suppl 1):S1-170.