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Review Article

The Impact of COVID-19 on the Prevalence, Mortality, and Associated Risk Factors for Mortality in Patients with Hip Fractures: A Meta-Analysis

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Hip fracture
COVID-19
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A B S T R A C T

Objective: This study aimed to assess (1) the prevalence of COVID-19 in patients with hip fracture; (2) the mortality rate of patients with hip fracture associated with COVID-19; (3) risk factors associated with mortality in patients with hip fracture; and (4) the effects of COVID-19 on surgical outcomes of patients with hip fracture.
Design: Meta-analysis.
Setting and Participants: Patients with hip fractures during COVID-19.
Methods: PubMed, Web of Science, and Embase were systematically reviewed. The outcomes included the prevalence of COVID-19, case fatality rate, 30-day mortality, cause of death, risk factors associated with the mortality of patients with hip fracture, time to surgery, surgical time, and length of hospitalization. Risk ratio or weight mean difference with 95% confidence intervals were used to pool the estimates.
Results: A total of 60 studies were included in this meta-analysis. The pooled estimate showed that the prevalence of COVID-19 was 21% in patents with hip fractures. Patients with hip fracture with COVID-19 had an increased 30-day mortality risk compared with those without the infection. The main causes of death were respiratory failure, COVID-19–associated pneumonia, multiorgan failure, and non–COVID-19 pneumonia. The hospitalization was longer in patients with COVID-19 when compared with those without the infection, but was shorter in patients during the pandemic period. The surgery time and time to surgery were not significantly different between patients during or before the pandemic period and in those with or without COVID-19.
Conclusions and Implications: The 30-day mortality rate was significantly higher in patients with hip fracture with COVID-19 infection than those without. Patients with COVID-19 had a higher all-cause mortality rate than those without. This information can be used by the medical community to guide the management of patients with hip fracture with COVID-19.
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Approximately 165 million infections and 3.4 million deaths were reported due to COVID-19 worldwide as of May 21, 2021.[1] As a result, the organization and delivery of health care services were affected worldwide. Analyses of cases showed that older people accounted for a higher percentage of COVID-19 deaths.[2] Moreover, there is evidence that the infection fatality rate increases with age, reaching 11.6% in patients older than 75 years.[3,4]

Hip fracture is one of the most common injuries in older patients, accounting for a high mortality risk.[5] Interestingly, there has been a demographic change in patients with hip fractures[6,7] because of the high postoperative mortality, limited mobility, and functional impairment that are associated with the surgical procedure.[5] Findings from previous studies showed a 30-day mortality rate of 5% to 7% among these patients[8] and nearly 25% within 1 year.[9] Higher mortality rates have been linked to several risk factors, including age, male gender, concomitant pathologies, surgical timing,[10] and COVID-19, which has emerged as a novel risk factor.[11,12]

L.D. and J.W. contributed equally to this manuscript.
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
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The global multicenter COVID-Surg Group demonstrated that the 30-day crude mortality rate for patients with COVID-19 would be as high as 29% perioperatively after an orthopedic surgery.[13] Moreover, the IMPACT group reported a crude 30-day mortality rate of 35% in patients with hip fracture, which increases threefold in patients with COVID-19 after controlling for confounders.[11] However, the IMPACT study was limited by a relatively small sample size (n = 27) of patients with COVID-19.[11] An additional limitation of this study was that it did not detail the time of COVID-19 diagnosis. This may have an impact on the mortality rate in COVID-19 groups with longer follow-up periods.

The impact of COVID-19 infection on hip fracture mortality was already studied by meta-analyses of clinical trials.[14-16] However, these reviews are limited by several potential factors, such as inconsistent inclusion criteria (from case series to multicenter studies), insufficient data for the analysis of adjusted mortality risk,[14] differences in the diagnosis time of COVID-19 and subsequent follow-up period,[15] publication bias,[16] and substantial heterogeneity in symptoms, interventions, and outcomes among included studies.[16] Furthermore, because clinical characteristics of patients infected with the Omicron subvariant have partly changed, an update of the current evidence is needed.

Therefore, the aim of this meta-analysis and systematic review was to evaluate (1) the prevalence COVID-19 in patients with hip fracture; (2) the mortality rate of patients with hip fracture associated with COVID-19; (3) risk factors associated with the mortality rate of patients with hip fracture; and (4) the effects of COVID-19 on surgical outcomes of patients with hip fracture.

Methods

Search Strategy

This study was performed in compliance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement guidelines.[17] The following terms were used in a comprehensive literature search in PubMed, Embase, the Cochrane Library, and Web of Science: “SARS-CoV-2”, “COVID”, “COVID-19”, “severe acute respiratory syndrome virus”, “coronavirus”, “hip fracture”, “trochanter fracture”, “femur neck fracture”, “collum femoris fracture”, “intertrochanteric fracture”, and “proximal femoral fracture”. The search included only studies in humans, and was restricted to original studies published in peer-reviewed journals in English. The reference list of identified papers and review articles were manually checked for additional relevant articles. Literature was searched from inception to July 21, 2022. Two independent investigators screened the abstracts for eligible articles and then reviewed the full text of the remaining articles. Disagreements were resolved by a third investigator. If several articles used the same population, we only included the trial with complete data.

Selection Criteria

We included clinical trials (including randomized controlled trials, cohort studies, and case-control studies) exploring the impact of COVID-19 on hip fracture epidemiology and 30-day mortality rates. To be included, studies needed to report either risk ratios (RR) with their 95% confidence interval (CI) or sufficient information to recalculate crude RRs with 95% CIs. Studies were excluded if there was no comparison between the pandemic period and the period before COVID-19, or if they were letters, reviews, or case reports.

Of note, when SARS-CoV-2 was in its peak in China’s Hubei province, patients were diagnosed as COVID-19 pneumonia (COVID-19+) according to relevant symptoms, significant epidemiological history, and typical computed tomography chest findings, without the need of laboratory confirmation. When reverse transcriptase-polymerase chain reaction (RT-PCR) was used for the diagnosis of SARS-CoV-2, patients were considered COVID-19+ or COVID-19− depending on the RT-PCR of their nasal or throat swabs. Patients who had strong clinical suspicion were considered to be COVID-19 suspect in spite of a negative swab test. For data analysis, suspect patients were included in the COVID-19+ group. Patients without pulmonary symptoms without swab tests were included in the COVID-19− group.

Data Extraction

Two independent investigators used a standardized form to extract data from each study. The extracted data included the following: first author, publication year, country, study design, sample size, population characteristics [age, gender, body mass index (BMI), comorbidities, fracture type, mean American Society of Anesthesiologists (ASA) Grade], definition of COVID-19 infection, diagnostic methods for COVID-19 test, confounding factors used, covariates used for multivariable adjustment (if any), RRs and 95% CIs, and outcomes (COVID-19 prevalence, 30-day mortality rate, case fatality ratio, characteristics of patients with hip fracture, mean duration of hospital stay, time to surgery, predictors of 30-day mortality, cause of death).

Quality Assessment

The methodological quality of non-randomized trials was assessed with the modified Newcastle-Ottawa scale (NOS).[18] This was based on 3 aspects: selection of study groups, comparability of the groups, and ascertainment of the outcome of interest. Scores ranged from 1 to 9, and studies with scores of 5 or more were considered high-quality studies.[18]

Statistical Analysis

Dichotomous variables were estimated using RRs and their 95% CIs, and continuous variables were calculated by the weight mean difference (WMD) method with 95% CIs. The heterogeneity among included studies was evaluated using the Cochrane’s Q test and estimation of I^2 statistic, in which $P < .1$ or $I^2 > 50\%$ was deemed significant.[19] When significant heterogeneity was identified, a random-effect model[20] was used for data analysis; otherwise a fixed-effect model[21] was applied. A meta-regression analysis was performed to investigate the impact of several factors [study design, percentage of females, age, BMI, ASA grade, and Nottingham hip fracture score (NHFS)] on the overall estimate if data were available. A sensitivity analysis[22] was performed to explore potential sources of heterogeneity by omitting each individual study separately. Publication bias was screened using the Egger’s and Begg tests.[23,24] All meta-analyses were performed using Review Manager 5.3 (Cochrane Collaboration) and STATA 14.0 (STATA Corp).

Results

Study Selection

The selection of included papers is presented in Figure 1. The initial search yielded 427 records, of which 294 were removed because of duplicates. Then, 133 papers were screened for title/abstract review, and 47 of them were excluded because of various reasons, leaving 86 potentially relevant articles for full-text review. A total of 26 studies were excluded: 4 were single-arm studies, 3 did not provide available data, 17 included outcomes out of our interest, and 2 included patients with other bone fractures. Finally, 60 observational studies,[11,12,25-82] including 57 cohort studies, and 3 case-control studies were included.

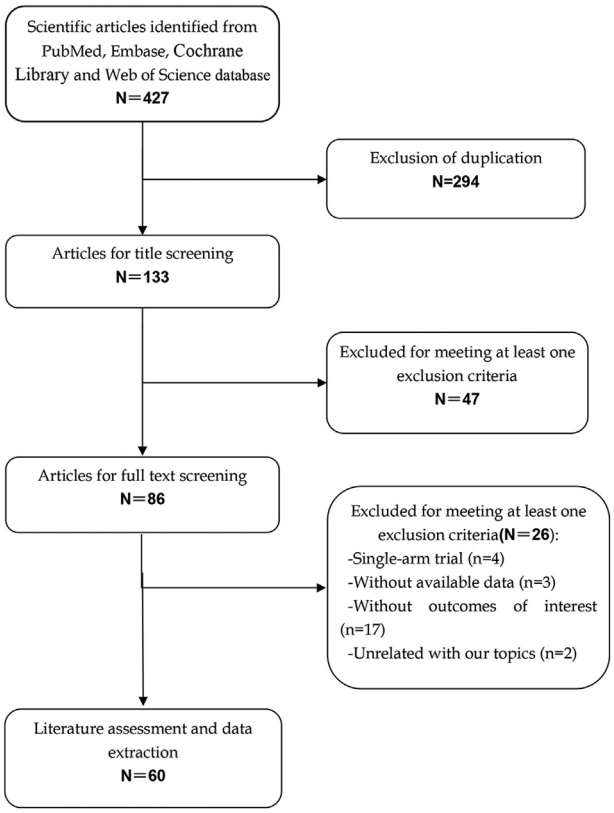

Fig. 1. Eligibility of studies for inclusion in the meta-analysis.

Characteristics of Eligible Studies and Quality Assessment

Table 1 shows the baseline characteristics of eligible studies. Studies were conducted primarily in the United Kingdom, followed by Israel, Italy, Chile, and Spain. The pandemic period in most included studies consisted of a period between March and May 2020. There were 204,570 participants in the included studies and studies differed in sample size from 47 to 91,160. All enrolled patients were ≥60 years of age. A methodological quality assessment was carried out on included studies using NOS, in which 14 studies had a score lower than 5 points (poor quality, high risk of bias) and 46 studies had a score higher than 5 points (good quality, low risk of bias). It is possible that selection and timing biases may be present in our analysis because the included studies used different COVID-19 testing protocols and study periods. Therefore, the prevalence of included studies does not represent the true prevalence of patients in this period.

Prevalence of COVID-19 in Patients With Hip Fracture

All included studies reported information on patients with COVID-19; however, only 31[11,12,25,31,33-37,40,47,54-57,60,63-66,73,74,76,77,79-81] of them provided sufficient data for analysis. Within 61,229 patients included in the abovementioned studies, we found that 21% (95% CI, 15%–28%) of patients were infected with COVID-19 (Figure 2).

Demographics of Patients With Hip Fracture

All included studies reported demographic characteristics of patients with hip fracture during and before the pandemic period. The mean age of these patients during and before the pandemic time was 78.32 ± 8.77 years and 82.37 ± 9.13 years, respectively. Pooled data showed that the age of patients with hip fracture was similar in both periods (WMD = 0.36 years; 95% CI, −0.20 to 0.92; $P = .210$). In contrast, the average age of COVID-19–infected patients with hip fracture was significantly higher than that of noninfected patients (WMD = 1.99 years; 95% CI, 1.53–2.45; $P < .001$).

Pooled data showed that the BMI between patients during and before the pandemic period was not significantly different (WMD = −0.08; 95% CI, −0.45 to 0.29; $P = .327$). In parallel, patients with hip fracture with COVID-19 infection had a similar BMI than patients without the infection (WMD = 0.37; 95% CI, −0.11 to 0.85; $P = .463$).

The ASA grades of patients during and before the pandemic period (WMD = 0.12; 95% CI, −0.01 to 0.25; $P = .716$), as well as the comparison of patients with or without COVID-19 (WMD = 0.11; 95% CI, −0.12 to 0.34; $P = .553$) were not significantly different.

Similar to ASA grades, the Charlson comorbidity index was also similar in the between-period (WMD = 0.10; 95% CI, −0.62 to 0.81; $P = .828$) and the infected vs noninfected comparisons (WMD = 0.04; 95% CI, −0.29 to 0.37; $P = .791$).

The abbreviated mental test (AMT) score is a screening tool consisting of 10 questions and was widely used to identify mental and functional preoperative status. Interestingly, although the mean AMT score was similar in patients before or during the pandemic period (WMD = 0.00; 95% CI, −0.73 to 0.73; $P = 1.00$), the mean AMT score in patients with hip fracture with COVID-19 infection was lower than that of patients without the infection (WMD = −2.03; 95% CI, −3.84 to −0.21; $P = .028$).

Finally, the mean NHFS was also similar between periods (WMD = 0.28; 95% CI, −0.06 to 0.62; $P = .715$) as well as for patients regardless of infection status (WMD = 0.24; 95% CI, −0.23 to 0.71; $P = .697$).

30-Day Mortality

Thirty-nine studies[11,25,30,31,33,34,36,37,39,40,43,46-48,50-52,54-56,60,62,63,65-69,71,73,74,76-81] reported data on 30-day mortality. Patients with and without COVID-19 infection had a 30-day mortality rate of 24.29% and 6.44%, respectively. The aggregated result demonstrated that the 30-day mortality rate for patients with hip fracture with COVID-19 infection was significantly higher than for that of noninfected patients (RR = 3.97; 95% CI, 3.20–4.92; $P < .001$) (Figure 3). The test for heterogeneity was significant ($I^2 = 71.8\%$, $P < .001$); however; neither the overall estimate (RR = 3.94; 95% CI, 2.53–6.14; $P < .001$) nor heterogeneity ($I^2 = 70.3\%$, $P < .001$) were affected by excluding the outlier trial.[66] A similar estimate (RR = 4.14; 95% CI, 2.50–6.86; $P < .001$) and heterogeneity ($I^2 = 72.4\%$, $P < .001$) were obtained after excluding the small sample size trial.[59]

We found a 12.20% 30-day mortality rate during and a 9.64% rate before the pandemic period in patients with hip fracture. Indeed, patients treated during the pandemic period had a significantly higher 30-day mortality than those treated pre-pandemic (RR = 1.32; 95% CI, 1.05–1.67; $P = .018$) (Figure 4). Significant heterogeneity was also found ($I^2 = 50.7\%$, $P = .001$), but the overall estimate (RR = 1.28; 95% CI, 1.02–1.62; $P = .036$) and heterogeneity ($I^2 = 51.0\%$, $P = .001$) did not change significantly upon outlier.[81]The overall estimate (RR = 1.29; 95% CI, 1.03–1.63; $P = .028$) and heterogeneity ($I^2 = 50.4\%$, $P = .001$) were not affected by the removal of the small sample size trial.[60]

Case Fatality Rate for Patients With COVID-19

Thirty-eight studies[11,12,25,26,28,30,33-37,40,47,48,50,51,53-57,59-61,65-68,71,73,76,77,79-82] reported data on case fatality rate. A case fatality rate between 0.6% and 82.3% was found among included studies. The pooled estimate showed that the case fatality rate for patients with hip fracture infected with COVID-19 was 27% (95% CI, 23%–32%; $P < .001$) (Figure 5). The test for heterogeneity was significant ($I^2 = 97.0\%$, $P < .001$); however, there was no significant change in the overall

Table 1
Baseline Characteristics of Patients in the Trials Included in the Meta-Analysis

Study	Study Design	Country	Study Period	No. of Patients	Age, y (mean ± SD) or mean (range)	NOS Score
Hall AJ[11]	Cohort	UK	March 2020	317	85.8 ± 7.9	5
Clement ND[12]	Cohort	UK	March 1 to 19 April 19, 2020	1563	82.8 ± 9.8	6
Narang A[25]	Cohort	UK	March 1 and April 30, 2020	682	83	5
Slullitel PA[26]	Case-control	Argentina	December 2019 and May 2020	160	86 (79-91)	5
Dupley L[27]	Cohort	UK	March 1 and April 26, 2020	64	83	4
Barker T[28]	Cohort	UK	March 24 and April 22, 2020	125	83.7 ± 8.47	5
Sobti A[29]	Cohort	UK	March 1 to May 31, 2020	188	83.5	6
Malik-Tabassum K[30]	Cohort	UK	March 23 to November 5, 2020	158	84.3 ± 8.9	5
Rashid F[31]	Cohort	UK	March 23 to December 31, 2020	1108	82.0 ± 8.3	7
Bobin MI[32]	Cohort	China	January 1 to July 20, 2020	145	72 (66-81)	5
Zamora T[33]	Cohort	Chile	March 15 to August 30, 2020	162	82 (75-88)	5
Fernando G[34]	Cohort	Spain	March 15 to April 30, 2020	146	83.8 ± 11.9	4
LeBrun DG[35]	Cohort	USA	March 20 to April 24, 2020	143	85.8 (79.8-91.3)	5
Dallari D[36]	Cohort	Italy	March 8 through May 4, 2020	477	83.3 ± 0.9	5
Kayani B[37]	Cohort	UK	February 1 and April 20, 2020	422	71.9 ± 9.5	5
Shemesh S[38]	Cohort	Israel	March 1 and May 31, 2020	182	82.3 ± 7.8	5
Prosso I[39]	Cohort	Israel	March and April 2020	129	85 ± 7.3	5
Walters S[40]	Cohort	UK	February 17 to May 17, 2020	139	83.1 ± 11.1	5
Audrey CS[41]	Cohort	Brazil	March and December 2020	139	≥ 60 years	5
Wilk R[42]	Cohort	Poland	March 16 to March 15, 2021	529	≥ 50 years	5
Park C[43]	Cohort	UK	Mid-March 2020	78	84	4
O'Driscoll CS[44]	Cohort	Ireland	2020 and 2021	265	80.69	5
Morri M[45]	Cohort	Italy	March 1 and June 30, 2020	360	85	5
Macey ARM[46]	Cohort	UK	5-wk period from March 20, 2020	152	83 (73-87)	5
Steinfeld Y[47]	Cohort	Israel	February and December 2020	287	80.5 ± 8.58	5
Fadulelmola A[48]	Cohort	UK	March and April 2020	75	83.7	4
Karthikeyan P I[49]	Cohort	India	April 1 to May 31, 2020	88	82.7 ± 7.50	5
Maniscalco P[50]	Cohort	Italy	February 22 to April 18, 2020	290	81 ± 5.1	5
Arafa M[51]	Cohort	UK	March to May 2020	138	≥ 60 years	5
Craig J[52]	Cohort	UK	March 2020 until May 23, 2020	700	83 (76-88)	5
Waterman JL[53]	Cohort	UK	March 23 and May 5, 2020	65	80.31 (62-94)	4
Kenneth A. E[54]	Cohort	UK	February 1 and April 15, 2020	253	83.0 ± 10.2	5
Karayiannis PN[55]	Cohort	UK	March 18 to April 27, 2020	469	64.2 ± 21.7	5
Sadiq S[56]	Cohort	UK	March 23 to April 21, 2020, November to December 4, 2020, January 4 to January 31, 2021	57	80.9 ± 7.5	4
COVIDSurg Collaborative[57]	Cohort	International, multicenter	February 1 to April 30, 2020	1050	≥ 60 years	6
Vialonga MD[58]	Cohort	USA	March 2020 and March 2021	149	74.0 ± 21.0	5
Grassi A[59]	Case-control	Italy	January 1, 2019, to May 31, 2020	56	82.9 ± 7.1	4
Chui K[60]	Cohort	UK	March 2020	47	86.8 ± 6.4	4
Chung JW[61]	Cohort	Korea	January 2020 to July 21, 2020	234	78.1 ± 11.4	5
Popp D[62]	Cohort	Austria	March 15, 2020, to May 30, 2021	491	≥ 60 years	5
Ali M[63]	Cohort	UK	March and June 2020	178	85.6	5
Galivanche AR[64]	Cohort	USA	April 1 to December 1, 2020	42002	≥ 60 years	6
Levitt EB[65]	Cohort	USA	March 15 and December 31, 2020	3303	82.9 ± 7.9	6
LeBrun DG[66]	Cohort	USA	March 20 to April 24, 2020	59	86.5 ± 7.9	4
Bilgetekin YG[67]	Cohort	Turkey	March and June 2020	281	81.2 ± 8.8	4
De C[68]	Cohort	UK	March 1 and May 15, 2020	141	81.3	4
Topor L[69]	Cohort	USA	January 17 to July 2, 2020	59	82 ± 7.9	4
Paccou J[70]	Cohort	France	January to July 2019 and January to July 2020	91160	≥ 50 years	6
Kim KK[71]	Cohort	Korea	March 12 to March 11, 2021	340	79 ± 12.2	5
Ronel D[72]	Cohort	Israel	March 19 to June 18, 2020	77	82.5 ± 8	5
Chan G[73]	Cohort	UK	March 1 and April 30, 2020	746	86	5
Fell A[74]	Cohort	UK	March 23 to May 12, 2020	122	86 ± 7.85	5
Hall AJ[75]	Cohort	UK	March 1 to May 31, 2020	7090	81.8 ± 10.7	6
Boukebous B[76]	Cohort	France	2020	181	83.63 ± 9.89	5
Orfanos G[77]	Case-control	UK	March 23 to May 13, 2020	199	82.1 (62-102)	5
Golinelli D[78]	Cohort	Italy	January and May 2020	1204	84.3 ± 7.6	6
Malik-Tabassum K[79]	Cohort	UK	March to May 11, 2020	242	83.7 ± 8.8	5
Segarra B[80]	Cohort	Spain	February 1 to April 15, 2020	138	70.6 ± 17.1	4
Thakrar A[81]	Cohort	UK	March 15 to April 14, 2020	94	81.5 ± 11.0	4
Verity R[82]	Cohort	China	January 1 to February 25, 2020	44672	All ages	6

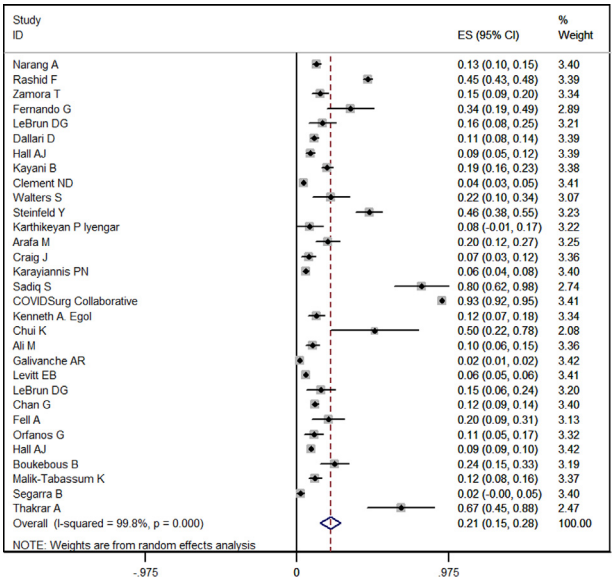

Fig. 2. Forest plot showing the prevalence of COVID-19 in patients with hip fracture.

estimate (ES = 26%; 95% CI, 21%–30%; $P = .001$) or heterogeneity ($I^2 = 96.9\%$, $P < .001$) when the outlier trial was excluded. Moreover, the overall data (ES = 27%; 95% CI, 23%–32%; $P < .001$) and heterogeneity ($I^2 = 97.0\%$, $P < .001$) were not affected by the exclusion of the small sample size trial.

Cause of Death

Almost all of the included studies reported the cause of death; however, only 13 studies[11,26,28,32,49-51,53,61,68,76,80,81] provided sufficient data for analysis. The main causes of death were respiratory failure, COVID-19 pneumonia, multiorgan failure, non–COVID-19 pneumonia, and heart failure (Table 2).

Other causes of death included acute coronary syndrome, brain hemorrhage, low gastrointestinal bleeding, pulmonary embolism, renal failure, frailty, septic shock, cancer, myocardial infarction, liver decompensation, and perforated ulcer (Table 2).

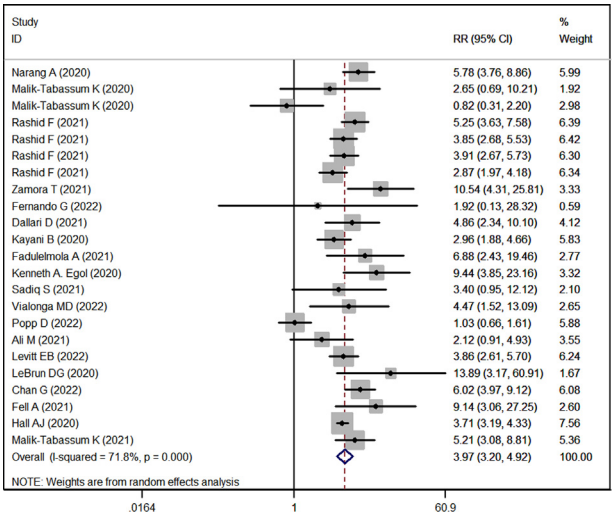

Fig. 3. Forest plot showing the comparison between patients who were COVID-19–positive and –negative in 30-day mortality rate.

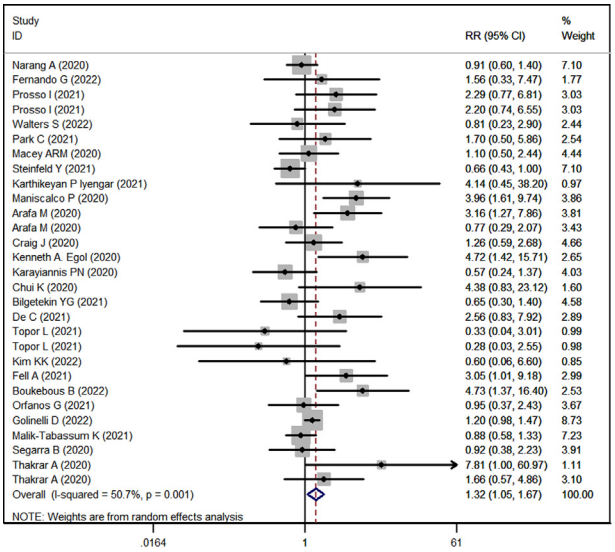

Fig. 4. Forest plot showing the comparison between patients during and before the pandemic in 30-day mortality rate.

Risk Factors of 30-Day Mortality in Patients With Hip Fracture

Seventeen studies[11,12,25,26,31,33,37,41,42,55,57,58,62,65,76,78] reported data on risk factors associated with hip fracture mortality. Confounding factors, such as gender and age, were adjusted for in these studies. The pooled data showed that COVID-19 infection, male gender, age (≥75 years), ASA grade (II–V), dementia, malignancy, medical comorbidities, renal disease, and pulmonary disease were risk factors for 30-day mortality in patients with hip fracture (Table 3). Other factors, including thromboembolic disease, Charlson comorbidity, instrumental activities of daily living score, delay (after 2 days), active smoking, and length of hospitalization >7 days, did not increase the 30-day mortality rate (Table 3).

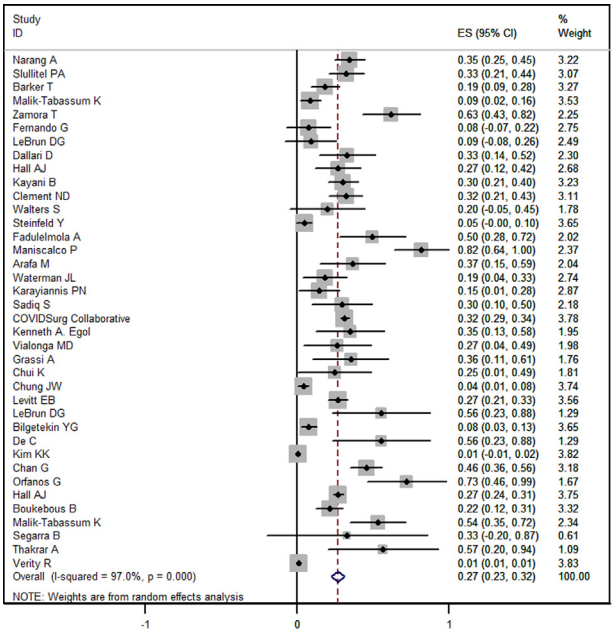

Fig. 5. Forest plot showing the comparison between patients who were COVID-19–positive and –negative in case fatality rate.

Table 2
Cause of Death for Patients With Hip Fracture

Cause	ES (95% CI)	*P*
Respiratory failure	50% (15.4% to 84.6%)	.005
COVID-19 pneumonia	38.7% (18.1% to 59.3%)	<.001
Multiorgan failure	27.3% (1.0% to 53.6%)	.042
Non–COVID-19 pneumonia	21.2% (9.5% to 33.0%)	<.001
Heart failure	8.5% (0.6% to 16.4%)	.034
Acute coronary syndrome	25% (−5% to 55%)	.102
Brain hemorrhage	1.6% (−0.9% to 4.1%)	.208
Low gastrointestinal bleeding	12.5% (−10.4% to 35.4%)	.285
Pulmonary embolism	16.7% (−4.4% to 37.8%)	.121
Renal failure	1.6% (−0.9% to 4.1%)	.216
Frailty	13.8% (−0.9% to 28.5%)	.066
Septic shock	3.1% (−0.2% to 6.5%)	.065
Cancer	3.0% (−0.4% to 6.5%)	.085
Myocardial infarction	16.6% (−13.9% to 47.0%)	.287
Liver decompensation	1.3% (−1.2% to 3.8%)	.314
Perforated ulcer	1.9% (−1.4% to 10.4%)	.562

Table 3
Risk Factors of 30-Day Mortality in patients With hip Fracture

Risk Factor	RR (95%CI)	*P*
COVID-19 infection	3.04 (2.40–3.86)	<.001
Male gender	1.29 (1.18–1.41)	<.001
Age (≥75 y)	2.79 (1.43–5.47)	<.001
ASA grade (II–V)	2.28 (1.28–4.05)	<.001
Dementia	2.01 (1.02–3.95)	.043
Malignancy	1.46 (1.16–1.83)	.001
Medical comorbidities	6.29 (1.16–34.04)	.033
Renal disease	1.42 (1.17–1.73)	.001
Pulmonary disease	1.45 (1.21–1.73)	<.001
Thromboembolic disease	1.81 (0.74–4.42)	.193
Charlson comorbidity	1.03 (0.91–1.16)	.652
IADL score	0.88 (0.17–4.57)	.876
Delay (after 2 d)	1.42 (0.81–2.50)	.22
Active smoking	4.13 (0.89–19.08)	.469
Length hospitalization >7 days	0.82 (0.50–1.35)	.427

IADL, instrumental activities of daily living.

Mean Surgery Time, Length of Hospitalization, and Time to Surgery

Eleven studies[11,26,28,30,31,33-41,45,47,49,51,53,54,56,58-61,63,66,67,69,71,72,77,79,80] reported data on surgical time. The mean surgery time in patients with hip fracture during and before the pandemic was 67.59 ± 24.51 minutes and 73.98 ± 20.75 minutes, respectively. The pooled analysis showed that there was no significant difference between the 2 groups (WMD = −1.86 minutes; 95% CI, −7.55 to 3.83; $P = .521$). Likewise, the surgery time was similar in COVID-19+ and COVID-19− patients (WMD = −5.86 minutes; 95% CI, −20.27 to 8.55; $P = .425$).

Fifteen studies[11,26,30,31,33-41,45,47,49,51,53,54,56,60,61,63,66,67,69,71,72,77,79,80] reported data on the length of hospitalization. The pooled data evidenced that hospital stays for patients with hip fracture during pandemic were significantly shorter than those of patients before the pandemic (WMD = −1.07 days; 95% CI, −1.89 to −0.26; $P = .01$). In parallel, patients with COVID-19 infection spent a significantly longer time in the hospital (WMD = 4.81 days; 95% CI, 2.91–6.70; $P < .001$).

Twenty-four studies[28-31,33,36,38,39,43,46,47,51,53,54,56,58-61,63,69,72,77,79] reported data on time to surgery. Surprisingly, the time to surgery for patients with hip fracture during the pandemic was similar to that of those before the pandemic (WMD = −0.05 days; 95% CI, −0.27 to 0.17; $P = .226$). Likewise, the time to surgery was similar in patients regardless of their infection status (WMD = 0.09 days; 95% CI, −0.12 to 0.31; $P = .287$).

Meta-Regression Analysis for 30-Day Mortality

Because of insufficient data, we only performed the meta-regression analysis for the effects of various potential risk factors on 30-day mortality. Results displayed in Table 4 show that only age ($P = .026$), BMI ($P = .008$), and ASA grade ($P = .011$) could predict the 30-day mortality among patients with hip fracture infected with COVID-19. None of these factors had an impact on 30-day mortality in patients during the pandemic.

Publication Bias

According to the Begg and Egger test, there was no evidence of publication bias for 30-day mortality (Begg: $Z = 1.07$, $P = .283$; Egger: $t = -1.04$, $P = .329$).

Discussion

In the present meta-analysis, we found that the prevalence of COVID-19 in patients with hip fracture was 21%, and the 30-day mortality risk was 3.97 times higher than in patients without COVID-19. Moreover, the case fatality rate was 27% for patients with hip fractures and COVID-19 concurrently, and the main causes of death were respiratory failure, COVID-19 pneumonia, multiorgan failure, and non–COVID-19 pneumonia. COVID-19 infection, male gender, age (≥75 years), ASA grade (II–V), dementia, malignancy, medical comorbidities, renal disease, and pulmonary disease were associated with increased 30-day mortality rates. Hospitalizations during the pandemic period were significantly shorter than those before the pandemic, but were longer for patients with COVID-19. The surgery time and time to surgery were not significantly different between patients during and before the pandemic period or those with or without COVID-19. Age, BMI, ASA grade, the Charlson comorbidity index, AMT score, and NHFS score were not significantly different between patients with hip fracture before and after the pandemic. COVID-19+ patients were older than COVID-19− patients.

The reported prevalence of COVID-19 in this study was 21%, which was lower than that reported by previous meta-analyses.[15,83] Lim et al.[83] included 6 studies with 984 participants, and reported a prevalence of 9% using a fixed-effects model and 16% using random-effects model. COVID-19 prevalence is proportional to the community prevalence, so it will depend on the population infection rate. In the United Kingdom, the prevalence of COVID-19 was 0.27% in April and May among the general population.[84] This review included studies primarily from the United Kingdom, which were performed between April and May 2020. Although data from March 2020 were also included, the population prevalence during that period was low.[84] We believe that the increased rate observed in this review may be related to the proportion of patients infected with COVID-19 on admission. Clement et al.[15] reported that the prevalence of patients with COVID-19 was 6.2% (n = 108 of 1721) upon admission and 64.9% (n = 200) after admission. In this context, it is important to protect vulnerable patients because the prevalence of COVID-19 in patients admitted with a hip fracture is approximately 23 times higher than that of the general population (prevalence on admission of 6.2% divided by general population prevalence of 0.27%).[15]

The case fatality rate observed in our study (27%) was substantially lower than that observed from China-based cases and deaths (3.67%).[82] A possible explanation for this discrepancy is that the severity of case is not considered in the crude estimate. For instance, we estimated the case fatality rate from different patient populations that included patients with mild symptoms[85] and hospitalized cases.[86] Interestingly, the case fatality rate in our review was lower than that observed in the meta-analysis by Raheman et al.,[16] which was 38.9%. These authors stated that the high case fatality rate might

Table 4
Results of the Multivariate Random-Effects Meta-Regression Analysis to Predict the Effects of Various Potential Risk Factors on 30-Day Mortality

Covariate	COVID-19 Positive vs COVID-19 Negative			During Pandemic vs Before Pandemic Period		
	Coefficient	95% CI	*P* Value	Coefficient	95%CI	*P* Value
Age	1.52	0.20 to 2.84	.026	0.39	−0.19 to 0.98	.179
Gender	−1.04	−0.41 to 1.98	.482	0.09	3.05 to 3.23	.955
BMI	−1.14	−3.27 to −0.99	.008	0.02	−1.27 to 1.32	.969
ASA grade	−3.05	−5.21 to −0.88	.011	0.07	−1.90 to 0.33	.892
NHFS	0.03	−1.99 to 2.05	.493	−0.79	−1.90 to 0.33	.159
Study design	NA	NA	NA	−1.63	5.49 to 2.23	.391

NA, not available.

be caused by studies conducted in the United States, specifically New York, in which the mortality risk of patients with hip fracture with COVID-19 was sixfold higher.[16] This region was the epicenter of the pandemic with a high COVID-19 infection rate and was influenced by associated hospital occupancy. This indicates that the pandemic has its impact through straining health care resources.

A patient's premorbid condition can be an independent predictor of adverse outcomes in hip fracture or COVID-19 infection. These patients are at greater risk of death because of their vulnerability. We identified several predictors, such as COVID-19 infection, male gender, age (≥75 years), ASA grade (II–V), dementia, malignancy, medical comorbidities, renal disease, and pulmonary disease. Indeed, the mortality rate of patients with COVID-19 with diabetes, hypertension, and cardiovascular disease was much higher than those of the general population.[54,87] Some studies reported that the trauma and surgical interventions also had an impact on the outcome of COVID-19.[88,89] As a result of skeletal injuries and surgical procedures, an inflammatory storm may develop, which may trigger a strong immune response induced by COVID-19.[88] The inflammatory storm is the most dangerous and potentially life-threatening event related to COVID-19, which might culminate in respiratory failure, kidney dysfunction, and cardiovascular events.[89]

In addition, extra precautions should be undertaken in these patients after their discharge, especially those classed as "vulnerable." Arafa et al.[51] reported that 2 patients from the COVID-19–negative group became COVID-19 positive after discharge back to their care homes. Then they were re-admitted within 30 days under the care of the Department of Medicine for the Elderly, and subsequently died with COVID-19 pneumonia. The patient's premorbid condition may increase the mortality risk; however, this should not have an impact on the decision to perform surgery because the surgical procedure can improve physiological ventilation, respiratory function, and overall stability of the patients. Therefore, surgery is urgently needed for these fragile subjects.[90,91] Numerous studies have demonstrated that delayed orthopedic care is closely associated with increased mortality.[91] As shown in the meta-analysis of Simunovic et al.,[92] surgery delayed beyond 48 hours is associated with an elevated risk of both mortality and prolonged hospitalization.

In this study, we found that COVID-19–positive patients with hip fracture had a worse clinical outcome and a higher mortality rate. It is therefore important to thoroughly evaluate the risks and benefits of urgent orthopedic surgery for patients with symptoms or who are at increased risk of infection. It is crucial to strike a balance between avoiding fracture-related complications that worsen cardiorespiratory function as well as the added stress from anesthesia and a fast-tracked procedure.[93] Although staff redeployment is needed, it is important to maintain adequate staffing on high-risk wards or areas. A faster response should be made that aims to improve screening test infrastructure, facilitate early discharge, and reduce hospital stays. In addition, more resources should be given to the highly vulnerable patients with hip fractures in the event of a new wave or future pandemic.

The current meta-analysis has some potential limitations. First, substantial heterogeneity was identified among the included studies, which might have affected the overall estimate. This is likely because of differences across included studies, such as the diagnosis of COVID-19 infection, type of anesthesia, use of anticoagulant, and timing of surgery. For instance, in some studies, patients were diagnosed with COVID-19 based on their nasal or throat swab test, regardless of their symptoms; whereas in other studies, patients were diagnosed according to a positive COVID-19 test and having symptoms. The diagnostic criteria for COVID-19 were different, leading to heterogeneity across studies. Meanwhile, in most studies, a combination of general and spinal anesthesia was used, whereas general anesthesia was used in other studies, which would lead to a higher mortality rate following the hip fracture surgery.[89] Deep vein thrombosis prophylaxis and anticoagulant type can also affect the mortality rate, but most studies did not report this information, thus we did not perform subgroup analyses. The time to surgery was also an important factor that might influence the mortality rate because a delay in surgery of more than 24 hours was shown to increase the mortality risk.[94] Second, in light of the limited data, we were unable to perform subgroup analyses based on SARS-CoV-2 types to explore whether different variants would result in different impacts on the mortality rate of patients with hip fracture. Third, this meta-analysis has a high risk of bias in some of the studies included (14 of 60 studies had a predetermined cutoff value of <6) and an uneven distribution of WMDs calculated for the respective outcome measures. Last, whether patients with hip fracture entered the hospital with or without COVID-19 was an important factor that might influence the outcomes; however, because of the insufficient information from included studies on this, we could not perform data analysis.

Conclusions and Implications

Altogether, the purpose of this review was to examine the impact of COVID-19 on hip fracture outcomes. The results of our study suggest that patients with hip fracture with COVID-19 infection had a significantly higher 30-day mortality rate than those without. Risk factors for 30-day mortality rate included COVID-19 infection, male gender, age (≥75 years), ASA grade (II–V), dementia, malignancy, medical comorbidities, renal disease, and pulmonary disease. This information may be useful for medical professionals that manage patients with COVID-19 with hip fractures.

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