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BJR

META-ANALYSIS

The prevalence, mortality, and associated risk factors for developing COVID-19 in hip fracture patients: a systematic review and meta-analysis

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Aims

The aims of this meta-analysis were to assess: 1) the prevalence of coronavirus disease 2019 (COVID-19) in hip fracture patients; 2) the associated mortality rate and risk associated with COVID-19; 3) the patient demographics associated with COVID-19; 4) time of diagnosis; and 5) length of follow-up after diagnosis of COVID-19.

Methods

Searches of PubMed, Medline, and Google Scholar were performed in October 2020 in line with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement. Search terms included "hip", "fracture", and "COVID-19". The criteria for inclusion were published clinical articles reporting the mortality rate associated with COVID-19 in hip fracture patients. In total, 53 articles were identified and following full text screening 28 articles satisfied the inclusion criteria.

Results

A total of 28 studies reported the mortality of COVID-19-positive patients, of which 21 studies reported the prevalence of COVID-19-positive patients and compared the mortality rate to COVID-19-negative patients. The prevalence of COVID-19 was 13% (95% confidence interval (CI) 11% to 16%) and was associated with a crude mortality rate of 35% (95% CI 32% to 39%), which was a significantly increased risk compared to those patients without COVID-19 (odds ratio (OR) 7.11, 95% CI 5.04 to 10.04; $p < 0.001$). COVID-19-positive patients were more likely to be male (OR 1.51, 95% CI 1.16 to 1.96; $p = 0.002$). The duration of follow-up was reported in 20 (71.4%) studies. A total of 17 studies reported whether a patient presented with COVID-19 (n = 108 patients, 35.1%) or developed COVID-19 following admission (n = 200, 64.9%), of which six studies reported a mean time to diagnosis of post-admission COVID-19 at 15 days (2 to 25).

Conclusion

The prevalence of COVID-19 was 13%, of which approximately one-third of patients were diagnosed on admission, and was associated with male sex. COVID-19-positive patients had a crude mortality rate of 35%, being seven times greater than those without COVID-19. Due to the heterogenicity of the reported data minimum reporting standards of outcomes associated with COVID-19 are suggested.

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Keywords: Hip, Fracture, Mortality, COVID-19, Outcome

Article focus

- The prevalence of coronavirus disease 2019 (COVID-19) in hip fracture patients and the associated mortality rate and risk associated with a positive diagnosis of COVID-19.
- The patient demographics, rate and time of acquiring COVID-19 after presentation, and assessment of whether the length of follow-up after diagnosis of COVID-19 was acceptable.

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Key messages

- The prevalence of COVID-19 in hip fracture patients was 13%, which was associated with a seven-fold increased mortality risk.
- The reporting of length of follow-up and follow-up from time of diagnosis of COVID-19 was not adequate and the need for minimum reporting standards is suggested.
- Confounding factors associated with mortality risk after hip fractures, such as sex, need to be accounted for when reporting the mortality risk of COVID-19.
- The timing (admission vs seven, 14, or 21 days following admission) at which a patient developed COVID-19 was associated with a profound effect on 30- and 60-day mortality rates following admission for hip fracture.

Strengths and limitations

- Reliable prevalence of COVID-19 in hip fracture patients at the height of the pandemic and the associated crude mortality rate.
- Limited data regarding the adjusted mortality risk, length of follow-up, and time at which COVID-19 was diagnosed, as well as the subsequent follow-up period.

Introduction

Hip fragility fracture patients are some of the oldest and most vulnerable group of patients presenting to orthopaedic services. The associated 30-day mortality after a hip fracture is approximately 5% to 8%.[1,2] Maintaining high medical and surgical standards has been shown to reduce early 30-day mortality.[3] There are numerous risk factors associated with an increased early mortality rate such as male sex, older age, comorbidities, independence, and place of residence.[4,5] However, the new risk factor that needs to be recognized is coronavirus disease 2019 (COVID-19), which has been reported to be independently associated with an increased early mortality rate in hip fracture patients.[6,7]

Mortality data from the global multicentre COVIDSurg group suggest the 30-day crude mortality rate may be as high as 29% for patients acquiring COVID-19 perioperatively after orthopaedic surgery.[8] The IMPACT group assessed the effect of COVID-19 on hip fracture patients, finding a crude 35% mortality rate at 30 days. They also quantified the associated increased mortality risk that was approximately three times greater in COVID-19-positive patients when adjusting for confounding factors.[6] A limitation of the IMPACT study was the relatively low number of COVID-19-positive patients (n = 27).[6] A further limitation of studies reporting on the mortality rate associated with COVID-19 after surgery is the detailing of the time a patient acquired COVID-19, i.e. pre- or post-admission, and if following admission what timepoint this was. This may influence the reported 30-day mortality associated with COVID-19 following injury, e.g. inclusion criteria to the COVIDSurg study was a diagnosis of COVID-19 any time within the 30-day post-operative follow-up period.[8] Therefore, if a patient were to acquire a diagnosis of COVID-19 on day 29 following surgery and survived one day, they would be categorized as a survivor of hip fracture surgery and COVID-19 and yet they may succumb to COVID-19 in the ensuing 28 days. This inconsistent practice in reporting follow-up after admission rather than after diagnosis of COVID-19 may result in a greater mortality rate in the COVID-19 group with longer follow-up. This is supported by two studies that followed up patients with COVID-19 beyond 30 days from admission and demonstrated an increased mortality rate,[7,9] which may in part be due to those being diagnosed late in their admission succumbing to the effects of COVID-19.

The aims of this systematic review and meta-analysis were to assess: 1) the prevalence of COVID-19 in hip fracture patients during the first wave of the pandemic; 2) the associated rate and risk of mortality compared to those without COVID-19; 3) the demographics associated with COVID-19-positive patients; 4) the time from the day of admission to diagnosis of COVID-19; and 5) length of follow-up after a diagnosis of COVID-19.

Methods

Searches of Medline, PubMed, and Google Scholar were performed in October 2020 in line with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.[10]

All identified article titles and abstracts were screened independently by two authors (NDC, CJS), with those meeting the inclusion criteria screened further by full text review. On occasions when it was not clear from the abstract if studies were of relevance, the full text of the article was reviewed. Unanimous consensus was met on the inclusion of proposed studies for full text review among the authors (NDC, CJS, RFLP). Full text studies were further evaluated against the inclusion and exclusion criteria. The reference lists of included studies were reviewed to ensure no other relevant studies were overlooked.

Search terms and criteria for inclusion. Search terms included ('hip' [All fields] OR 'mortality' [All fields] OR 'fracture' [All fields] OR 'COVID-19' [MeSH terms]) with all entry terms. A search limit for articles published from 2020 was applied. A single search of PubMed (n = 52) and Medline (n = 44) yielded 96 abstracts. Two searches of Google Scholar using the search terms (1) allintitle: hip COVID-19 (n = 56) or coronavirus (n = 6) yielded 59 articles (three identical studies). A further seven articles were identified from references. The criteria for inclusion were published clinical research articles reporting: 1) the rate of COVID-19 (at admission or following admission) in patients with a hip fracture and 2) the associated mortality

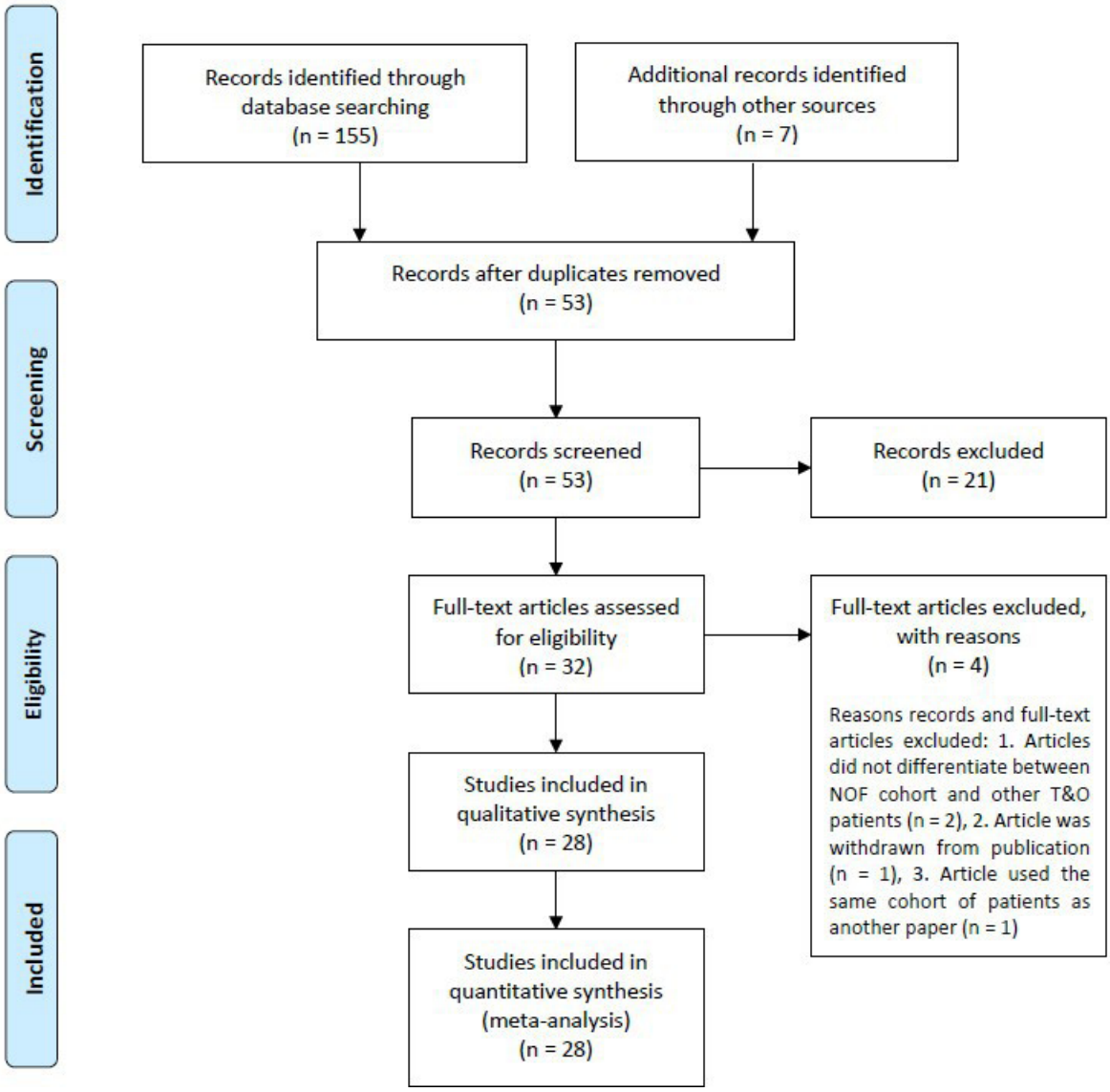

Fig. 1

Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram for the studies identified and included in the review. NOF, neck of femur fracture; T&O, Trauma and Orthopaedics.

rate. Studies were excluded if they were case reports, review articles, conference abstracts, non-clinical studies, or were not available in the English language (n = 0). For the purpose of this review, if data regarding the mortality rate in a comparative group without COVID-19 were available, they were recorded.

Data extraction. The included studies were evaluated for the authors, year of publication, title, where it was published, study design (prospective or retrospective), age and sex of patients, number of patients, length of follow-up, number of COVID-19-positive patients and mortality rate, the time of diagnosis of COVID-19 (on admission or following admission with mean time to diagnosis), number of COVID-19-negative patients and mortality rate (if reported), and what adjustments were made for confounding factors on mortality risk between those with and without COVID-19. A positive diagnosis was defined as those patients testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on swab testing (antigen polymerase chain reaction test) or a positive serum SARS-CoV-2 antibody test, or if they were assigned a clinical diagnosis on clinical signs and imaging.

Outcome measures. The primary objectives were to report the prevalence of COVID-19 in hip fracture patients during the first wave of the pandemic (March to July 2020), the associated rate and risk of mortality, time of acquiring COVID-19 after presentation, and length of follow-up after diagnosis of COVID-19. Secondary objectives included presenting the demographic data (age and

Table I. Studies included in the systematic review according to coronavirus disease 2019 status.

Author	Design	No. of patients	Follow-up, days	COVID-19-positive patients								Non-COVID-19 patients				
				N	Deaths, n	Females, n	Mean age, yrs (SD)	Mortality, %	No. at admission	No. after admission	Time to dx, days†	N	Deaths, n	Females, n	Mean age, yrs (SD)	Mortality, %
Arafa[36]	RETRO	97	30	19	7	10	86.2 (7.7)	36.8	?	?	?	78	7	57	83.1 (7.6)	9
Catellani[37]	RETRO	16	?	16	7	6	84.3 (4.4)	43.8	?	?	?	N/A	N/A	N/A	N/A	N/A
Cheung[38]	RETRO	10	?	10	1	8	79.7 (6.7)	10.0	7	3	5, 8, & 9	N/A	N/A	N/A	N/A	N/A
Chui[39]	RETRO	47	?	8	4	?	?	50.0	?	?	?	39	1	?	?	2.6
Clement[7]	RETRO	354	50	47	17	?	?	36.2	4	43	?	307	50	?	?	16.3
Clough[40]	RETRO	84	?	7	5	3	85.1‡	71.4	0	7	?	77	13	49	80.0‡	16.9
De[41]	RETRO	276	30	34	14	22	85.9 (7.7)	41.2	?	?	?	242	?	?	?	N/A
Dupley[9]	RETRO	64	30	64	21	35	83 (9.0)	32.8	12	52	?	N/A	N/A	N/A	N/A	N/A
Egol[42]	PROSP	138	30	31	11	15	81.6 (9.9)	35.5	?	?	?	107	6	73	83.4 (10.4)	5.6
Fadulelmola[18]	RETRO	75	30	20	10	13	83.7‡	50.0	6	14	mean 13	55	4	40	83.5‡	7.3
Hall[6]	RETRO	317	30	27	9	13	83.6 (11.3)	33.3	6	21	?	290	24	198	80.4 (10.6)	8.3
Karayiannis[19]	RETRO	203	30	21	4	?	?	19.0	?	?	?	182	3	?	?	1.6
Kayani[20]	RETRO	442	30	82	25	51	71.9 (9.5)	30.5	42	40	?	340	35	204	72.7 (6.7)	10.3
Lazizi[21]	RETRO	31	11.5	3	2	1	88 (5.2)	66.7	0	3	2, 4, & 14	28	0	?	?	0
LeBrun[22]	RETRO	59	?	9	5	6	86.5 (7.9)	55.6	7	2	?	50	2	38	84.7 (7.5)	4
Macey[23]	RETRO	76	30	10	2	?	?	20.0	1	9	mean 25	66	9	?	?	13.6
Malik-Tabassum[24]	RETRO	68	30	1	1	?	?	100.0	1	0	N/A	67	5	?	?	7.5
Maniscalco[25]	RETRO	121	21	32	14	?	?	43.8	?	?	?	89	3	?	?	3.4
Mi[26]	RETRO	6	30*?	6	3	4	75.7 (13.0)	50.0	2	4	mean 7	N/A	N/A	N/A	N/A	N/A
Muñoz Vives[27]	RETRO	136	10	23	7	?	?	30.4	?	?	?	113	6	?	?	5.3
Morelli[28]	RETRO	10	14 to 39	10	2	8	83.9 (7.4)	20.0	10	0	N/A	N/A	N/A	N/A	N/A	N/A
Muse[29]	RETRO	5	8 to 15	5	0	4	79 (8.2)	0.0	5	0	N/A	N/A	N/A	N/A	N/A	N/A
Narang[30]	PROSP	682	30	86	30	53	86‡	34.9	?	?	?	596	36	424	83.0‡	6
Rabie[31]	RETRO	4	?	4	2	3	81 (9.0)	50.0	3	1	?	N/A	N/A	N/A	N/A	N/A
Segarra[32]	PROSP	68	30	2	1	1	87.5‡	50.0	2	0	?	66	7	45	82.2‡	10.6
Sobti[33]	PROSP	94	?	6	3	?	?	50.0	?	?	?	88	6	?	?	6.82
Stoneham[34]	RETRO	48	?	1	0	?	?	0.0	0	1	20	47	0	?	?	0

*Probably 30 days follow-up but not clearly stated.
†Absolute number of days stated, unless a mean is given.
‡No SD available.
?, not recorded; COVID-19, coronavirus disease 2019; dx, diagnosis; N/A, not applicable; PROSP, prospective; RETRO, retrospective.

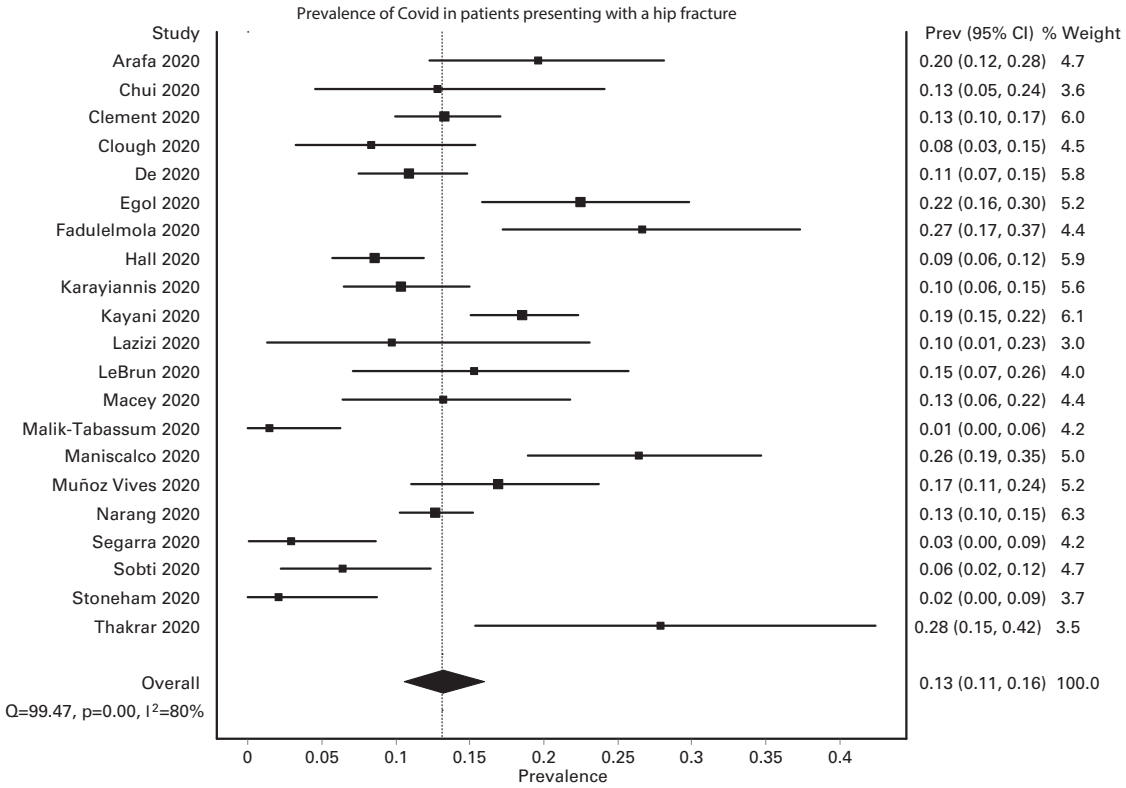

Fig. 2

Prevalence of coronavirus disease 2019 (COVID-19) according to the 21 studies that included data for COVID-19-positive and -negative patients. CI, confidence interval.

sex) and the methodology for reporting the mortality risk associated with COVID-19-positive patients (crude unadjusted vs adjusted).

Quality assessment. Using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies,[11] all included publications were reviewed independently for potential risk of bias by two authors (NDC, NN). The assessment tool uses 14 questions to enable allocation of a score to each article (poor, fair, or good). If there was disagreement regarding the scoring of a study, consensus was met after discussion among both assessors.

Statistical analysis. Simple descriptive analysis was performed for the five aims of the review. Heterogeneity among the studies was assessed using the chi-squared test and I^2, however due to suspected variation among the studies and associated heterogeneity random effects models were used for all meta analyses.[12] The mortality risk associated with COVID-19-positive compared to -negative patients and association with sex were statistically assessed using random effects models (DerSimonian and Laird),[13] and odds ratios (OR) were presented as the effect measure (Mantel–Haenszel). Whereas the association of age and risk of COVID-19 was assessed using a random effects model and the mean difference was presented as the effect measure (inverse variance). For each outcome variable, 95% confidence intervals (CIs) are presented. A p-value < 0.05 was considered statistically significant in cases in which trials have no event in one arm or another. The meta-analysis was conducted using Review Manager 5.2 (Cochrane Collaboration, Oxford, UK).

Results

There were 53 articles identified in the initial search of databases and reference lists (Figure 1). After initial screening of titles and abstracts 32 articles met the inclusion criteria for review. On full text screening a further four studies were excluded from analysis as they reported the rate of COVID-19 for a cohort of trauma patients and either did not declare the rate for hip fracture patients in isolation (n = 2),[14,15] reported the same cohort of patients in a prior included study (n = 1),[16] or was a retracted publication (n = 1)[17] (Figure 1). A list of the 28 studies that met the inclusion criteria are illustrated in Table I.[6,7,9,18–42] Of the 28 published studies identified, five (17.9%) were prospective[30,32,33,35,42] and the remainder were retrospective (Table I).

Prevalence of COVID-19 in hip fracture patients. A total of 21 of the included studies reported the rate of COVID-19-positive patients (n = 481) in a cohort of hip fracture patients, which included 3,439 patients in total.[6,7,18–25,27,30,32–36,39–42] The prevalence of COVID-19 ranged

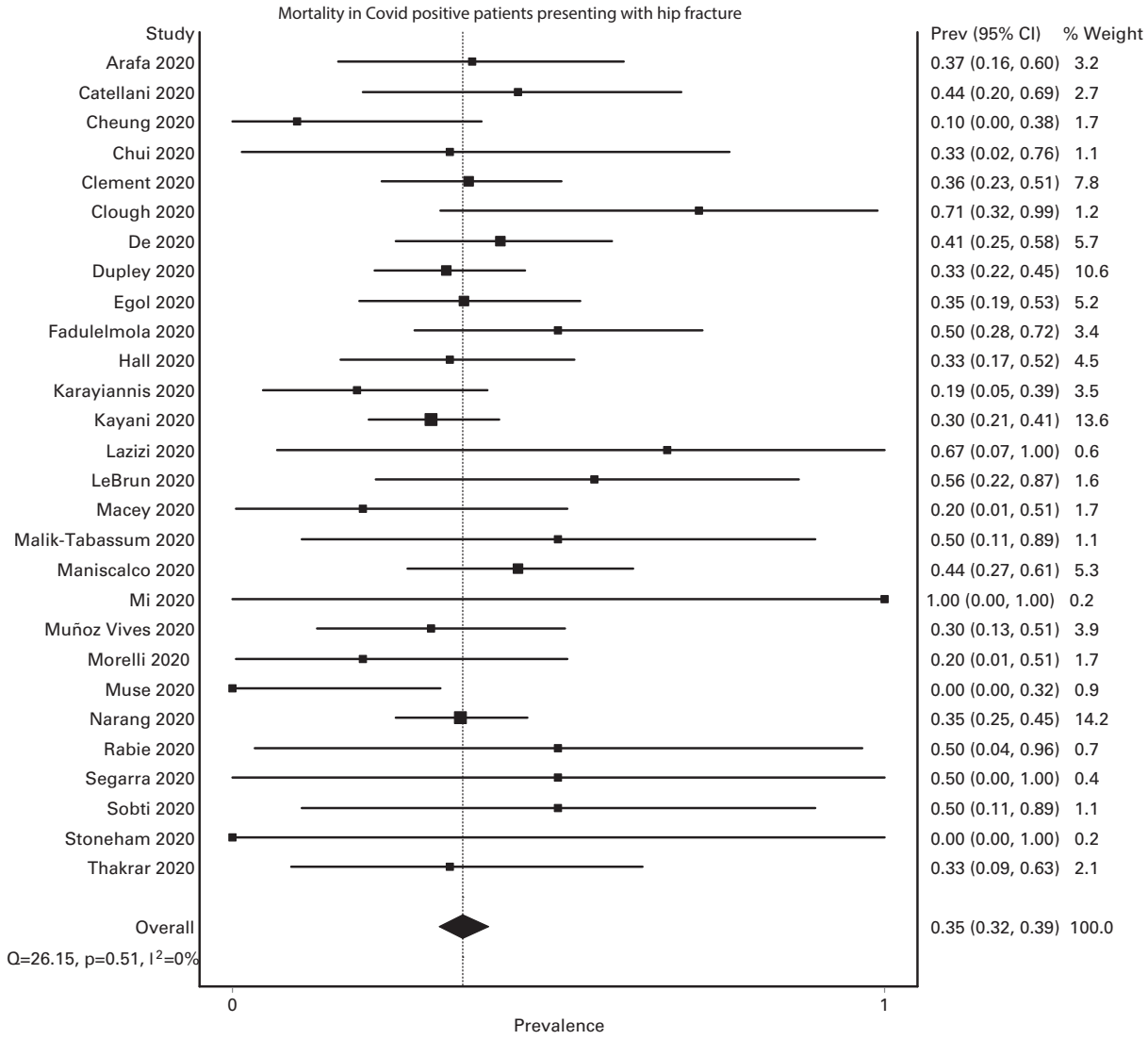

Fig. 3

Crude mortality rate of hip fracture patients with coronavirus disease 2019 (COVID-19) according to the 28 included studies. CI, confidence interval.

from 1% to 28%, with a mean of 13% (95% CI 11% to 16%) (Figure 2).

The rate and risk of mortality associated with COVID-19. All 28 studies included COVID-19-positive patients. In total, there were 596 COVID-19-positive patients of whom 211 (35.4%) were reported to be deceased.[6,7,9,18–42] The mortality rate ranged from 0% to 100%, with an overall crude unadjusted mortality rate of 35% (95% CI 32% to 39%) (Figure 3). There were 21 studies reporting the mortality rate in both COVID-19-positive and negative hip fracture patients, and meta-analysis of these data demonstrated a significantly increased risk of mortality in COVID-19-positive patients when compared to -negative patients with a hip fracture (OR 7.11, 95% CI 5.04 to 10.04; p < 0.001, Mantel-Haenszel) (Figure 4). [6,7,18–25,27,30,32–36,39–42]

Patient demographics (sex and age) for those who were COVID-19-positive or -negative were reported in nine (n = 9/21, 42.9%) of the 21 studies comparing the mortality rate between these two groups (Table I).[6,18,20,22,30,32,36,40,42] Of those reporting patient demographics, COVID-19-positive patients were older (mean difference of 1.8 years, 95% CI -0.9 to 4.6, p = 0.190, inverse variance) (Figure 5) and were significantly more likely to be male: 41.7% (n = 118/283) of COVID-19-positive patients versus 32.0% (n = 531/1,659) of those without a diagnosis of COVID-19 (OR 1.51, 95% CI 1.16 to 1.96, p = 0.002, Mantel-Haenszel) (Figure 6). Only two studies adjusted for confounding factors (including age and sex) associated with patient mortality and demonstrated an independent increased risk associated with COVID-19-positive patients with hazard ratios of 1.9 and 3.5.[6,7] A further limitation of the reported crude mortality rates was the poor reporting of the follow-up period assessed, with only 20 (71.4%) of the 28 studies reporting a follow-up time period that ranged from eight to 50 days with the majority (n = 14) reporting a 30-day follow-up (Table I).

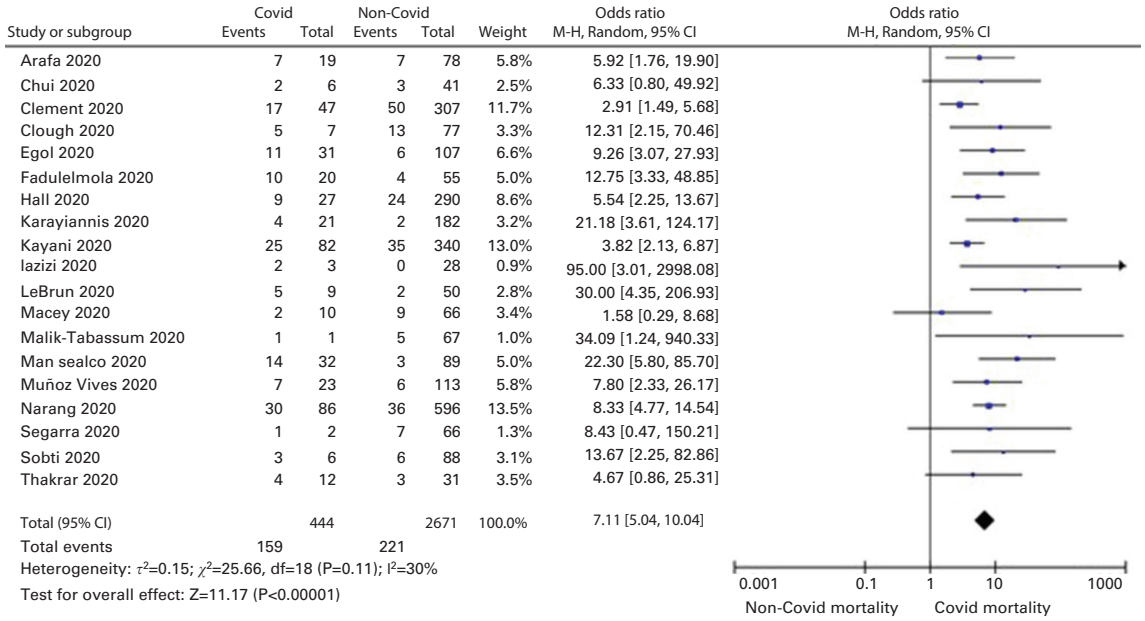

Fig. 4

Mortality risk associated with coronavirus disease 2019 (COVID-19) in hip fracture patients according to the 21 studies that included data for COVID-19-positive and -negative patients. CI, confidence interval; M-H, Mantel-Haenszel.

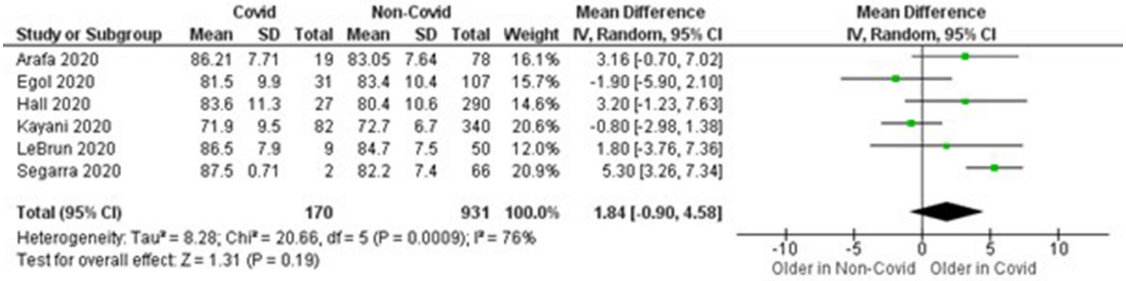

Fig. 5

Six studies that reported the age and SD of both coronavirus disease 2019 (COVID-19)-positive and -negative patients were in the meta-analysis, and assessed whether there was an association of age with a positive diagnosis of COVID-19 in hip fracture patients. CI, confidence interval; IV, inverse variance.

Time of acquiring COVID-19 and length of follow-up after diagnosis of COVID-19. All 28 of the included studies reported the mortality rate associated with COVID-19-positive patients (Table I). However, it was not clear what proportion had COVID-19 on admission or subsequently developed the diagnosis, with only 17 (60.7%) of the 28 included studies reporting when the patient acquired COVID-19 (Table I). There were 108 (35.1%) patients admitted with COVID-19 and 200 (64.9%) patients who subsequently developed COVID-19, i.e. the prevalence of COVID-19 on admission was 6.2% (n = 108/1,721) and the rate of developing COVID-19 following admission was 11.6% (n = 200/1,721). Six of the 17 studies reported the time to diagnosis of COVID-19 from admission,[18,21,23,26,34,38] which ranged from 2 to 25 days (Table I) with a combined mean time of 15 days. Three of these six studies did not declare an overall follow-up time for their cohort.[26,34,38] Of the other three studies, one had a minimum follow-up of 11.5 days and did not declare how long patients with COVID-19 were followed up for,[21] and the remaining two studies reported a 30-day follow-up after admission which resulted in a follow-up period after diagnosis of COVID-19 of between five and 17 days.[18,23]

Discussion

This review has demonstrated the prevalence of COVID-19 in hip fracture patients to be 13% during the first wave of the pandemic, and was associated with a crude mortality rate of 35% that was significantly increased compared to those without COVID-19 (8%). Furthermore, male sex was also found to be associated with an increased risk of acquiring COVID-19. Most patients were diagnosed with COVID-19 after their admission (n = 200, 64.9%) and the length of follow-up after diagnosis of COVID-19 acquired after admission was short (five and 17 days). There were a low rates of

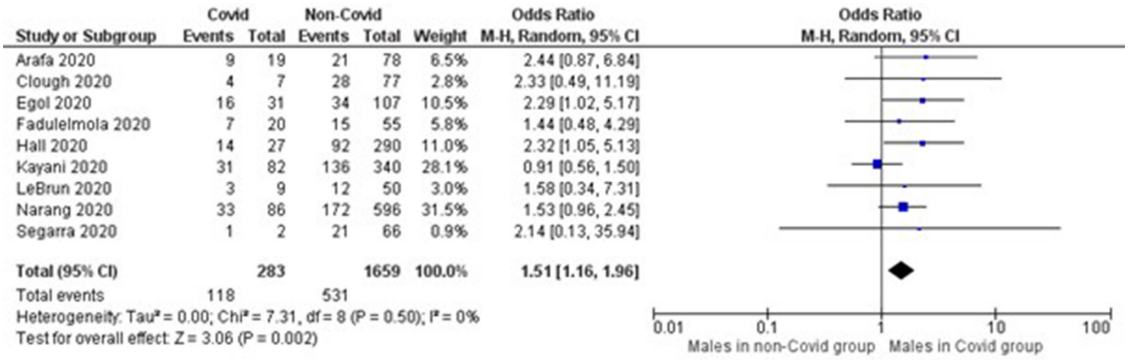

Fig. 6

Nine studies that reported the sex of both coronavirus disease 2019 (COVID-19)-positive and negative patients were in the meta-analysis, and were assessed for an association with a positive diagnosis of COVID-19 in hip fracture patients. CI, confidence interval; M-H, Mantel-Haenszel.

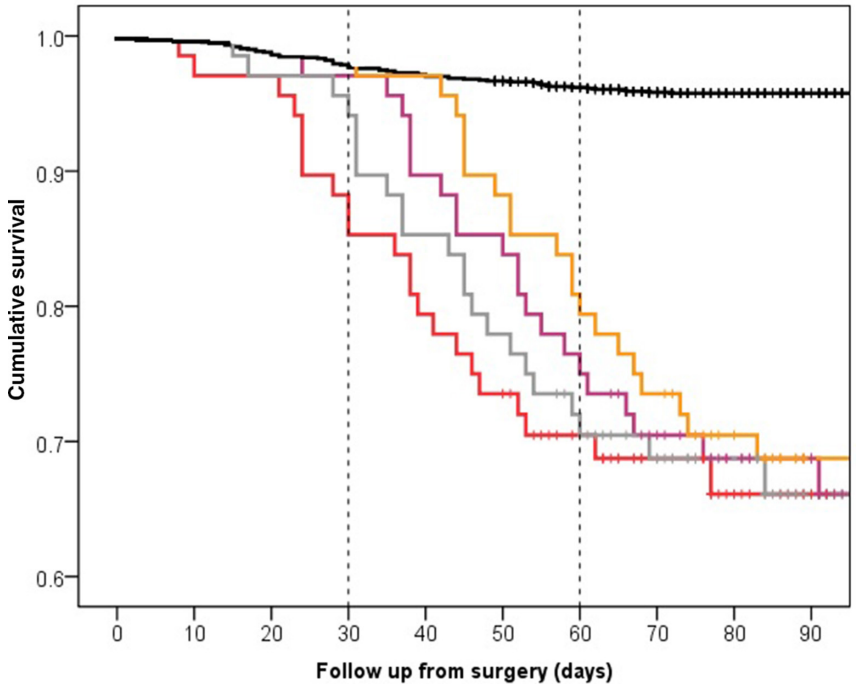

Fig. 7

Kaplan–Meier survival curves for patients with (n=68, red line) and without (n=1501, black line) perioperative coronavirus disease 2019 (COVID-19) perioperatively, using data from Clement et al.[7] The grey, purple, and orange lines indicate hypothesized seven, 14, and 21 day delays in time of acquiring COVID-19, respectively. This graph shows the effect on the rate of 30- and 60-day mortality rates, with an approximate variation of 10% in cumulative survival rates.

reporting in terms of the length of time patients were followed up (71.4%, n = 20/28 studies), description of patient demographics in comparative studies (42.9%, n = 9/21 studies), time at which COVID-19 was diagnosed (60.7%, n = 17/28 studies), and time at which those patients acquired COVID-19 post-admission (21.4%, n = 6/28 studies). The majority (n = 26/28, 92.9%) of studies reported the crude (unadjusted) mortality rate associated with COVID-19.

A limitation of the current review was the defined inclusion criteria for a COVID-19-positive patient, being either a clinical suspected diagnosis or a positive antigen test. This may have resulted in an overestimate of the prevalence of COVID-19 during the first wave. However, the majority of studies in the current review included test-positive patients, with only a few early reports using a clinical diagnosis of COVID-19. To have included only those patients who tested positive, the authors felt this would have not only resulted in a lower prevalence but may have increased the mortality rate. For example, Egol et al[42] reported 17 patients who were test-positive and a further 14 patients who were suspected of having COVID-19. Their overall mortality rate was 35%, being identical to that identified on meta-analysis in this study, however the mortality rate in test-positive patients was 53%.

Table II. Suggested minimum criteria for studies reporting the association of coronavirus disease 2019 and mortality.

Suggested reporting criteria
Demographics: age, sex*
Comorbidity*
Independence*
Minimum follow-up period for the cohort*
How the diagnosis of COVID-19 was assigned (clinical vs test)
How many patients were admitted with COVID-19
How many patients developed COVID-19 following admission
When the post-admission patients were diagnosed with COVID-19
Follow-up from time of diagnosis of COVID-19

*For both patients with and without coronavirus disease 2019, if reporting data for both cohorts.
COVID-19, coronavirus disease 2019.

The reported prevalence of COVID-19 in the current review of 13% during the first wave was similar to that reported by Lim and Pranata[43,44] in their meta-analysis, who demonstrated a 9% prevalence using a fixed effect analysis and a 16% prevalence using a random effects analysis. The prevalence of COVID-19 will likely be directly proportional to the community prevalence and will thus be dependent on the reporting centres' catchment population COVID-19 infection rates. The population prevalence of COVID-19 in April and May in England was estimated to be 0.27%, i.e. 1:400.[45] The majority of the studies included in the current review were from the UK and conducted during this time period of April and May 2020; March 2020 was also included but there are limited population prevalence data available for the UK during this month.[45] This community prevalence of 0.27% was far lower than the 13% prevalence observed in the hip fracture patients. In part this increased rate may be related to a proportion of patients acquiring COVID-19 after admission as the prevalence on admission was 6.2% (n = 108/1,721), with the majority (n = 200, 64.9%) of patients being diagnosed with COVID-19 after admission. This highlights the importance of pathways to protect these vulnerable patients who seem to have a higher prevalence of COVID-19 that is approximately 23 times greater than the background population prevalence when admitted with their hip fracture (prevalence on admission of 6.2% divide by population background prevalence of 0.27%).

Male sex was associated with developing COVID-19 in patients presenting with a hip fracture in this review. The association of COVID-19 and male sex was highlighted by Hall et al[6] in their cohort of 317 hip fracture patients, demonstrating an independent association with male sex and a positive diagnosis of COVID-19 with a OR of 2.3, being greater than the OR of 1.5 identified in the current study. Male sex has been recognized as a predisposing factor to acquiring COVID-19 infection and a greater mortality rate should it be acquired, relative to female sex.[46] The reasons for this predisposition and increased mortality rate are not clear. Sex hormones and the higher expression of angiotensin-converting enzyme-2, which is a receptor for SARS-CoV-2, in males have been suggested as possible mediators of predisposition to developing COVID-19.[46] Lifestyle factors such as smoking and alcohol consumption, along with attitudes towards the COVID-19 pandemic, have also been suggested as possible factors as to why COVID-19 is more prevalent in males relative to females.[46] Male sex is recognized as a risk factor that is associated with an increased risk of 30-day mortality following a hip fracture prior to the COVID-19 pandemic, and should be adjusted for when assessing factors associated with mortality.[4,5] As COVID-19 is more prevalent in males following a hip fracture, who also have a higher mortality risk following a hip fracture, it is important that future studies should account for this in their survival analysis rather than simply presenting the crude mortality rate.

The majority (92.9%, n = 26/28) of the studies included in the current review report a crude mortality rate for patients with a hip fracture and COVID-19, and did not adjust for confounding factors such as age, sex, comorbidity, or independence, which have all been demonstrated to influence 30-day mortality after a hip fracture.[4,5] Two studies adjusted for such confounding variables and demonstrated a hazard ratio of 1.8 and 3.5, i.e. patients developing COVID-19 were two to three-and-a-half times more likely to die than those patients without a diagnosis of COVID-19.[6,7] Whereas the pooled unadjusted mortality data from the current reviewd-emonstrated a greater mortality risk for COVID-19 patients with an odds ratio of 7.1, however odds ratios and hazard ratios are not the same and represent different risks.[47] This higher unadjusted odds ratio may also be due to other confounding factors; as patient factors were not considered and when correcting for these the adjusted mortality hazard ratio for COVID-19-positive patients may be reduced. This highlights the need for future studies to report both the crude unadjusted mortality rate and the adjusted rate for their population, or at least to present the demographics of the patients with and without COVID-19 (e.g. sex, age, American Society of Anesthesiologists (ASA) grade,[48] and independence). Nonetheless, hip fracture patients with concomitant COVID-19 have a minimum of a twofold increased mortality risk comparted to patients without COVID-19.

The current study has highlighted the poor reporting rates for the length of follow-up (71.4%, n = 20/28 studies), whether the patient was COVID-19-positive at admission (60.7%, n = 17/28 studies), and the time at which COVID-19 was diagnosed following admission (six studies). These criteria are important when reporting mortality associated with COVID-19 in any cohort of patients, i.e. to quantify the number of patients at risk over a defined time period. The majority (50%, n = 14/28) of studies in the review followed up patients for 30 days following admission, which is not the same as following

patients up to 30 days following diagnosis with COVID-19 as most patients develop this following their admission to hospital. If it is hypothesized that the survival rate after acquiring COVID-19 perioperatively is the same should COVID-19 be acquired 7, 14, and 21 days later, this had a profound effect on the potential mortality rates at 30 and 60 days (Figure 7).[7] To enable interpretation of such data, the authors suggest that future studies should include minimal reporting criteria when assessing the association of COVID-19 with mortality (Table II).

In conclusion, one in eight patients with a hip fracture during the first wave had COVID-19 at presentation or acquired it following their injury. COVID-19 was more prevalent in male patients and was associated with a 35% crude mortality rate that was greater than those without COVID-19. Minimum reporting criteria are needed for studies that report the association of COVID-19 on mortality in hip fracture patients, which would include: patient demographics; length of follow-up; time at which COVID-19 was diagnosed (at or post-admission); as well as a minimum of 30 days' follow-up after the diagnosis of COVID-19 and if possible an adjusted mortality rate/risk.

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References

1. **Holt G**, **Smith R**, **Duncan K**, **McKeown DW**. Does delay to theatre for medical reasons affect the peri-operative mortality in patients with a fracture of the hip? *J Bone Joint Surg Br*. 2010;92-B(6):835–841.
2. **Pincus D**, **Ravi B**, **Wasserstein D**, **et al**. Association between wait time and 30-day mortality in adults undergoing hip fracture surgery. *JAMA*. 2017;318(20):1994–2003.
3. **FarrowL**, **HallA**, **WoodAD**. Quality of Care in Hip Fracture Patients: The Relationship Between Adherence to National Standards and Improved Outcomes. *J Bone Joint Surg Am*. 2018;100-A:751–757.
4. **Maxwell MJ**, **Moran CG**, **Moppett IK**. Development and validation of a preoperative scoring system to predict 30 day mortality in patients undergoing hip fracture surgery. *Br J Anaesth*. 2008;101(4):511–517.
5. **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;106(4):501–504.
6. **Hall AJ**, **Clement ND**, **Farrow L**, **et al**. IMPACT-Scot report on COVID-19 and hip fractures: a multicentre study assessing mortality, predictors of early SARS-CoV-2 infection, and the effects of social lockdown on epidemiology. *Bone Jt J*. 2020;102-B(9):1219–1228.
7. **ClementND**, **HallAJ**, **MakaramN**, **et al**. IMPACT-Restart: the influence of COVID-19 on postoperative mortality and risk factors associated with SARS-CoV-2 infection after orthopaedic and trauma surgery. *Bone Joint J*. 2020;102-B(12):1774–1781.
8. **COVIDSurg Collaborative**. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. *Br J Surg*. 2020. (Epub ahead of print) PMID: 32395848.
9. **DupleyL**, **OputaTJ**, **BourneJT**, **North West COVID NOF Study Group**. 30-day mortality for fractured neck of femur patients with concurrent COVID-19 infection. *Eur J Orthop Surg Traumatol*. 2020:1–7.
10. **MoherD**, **LiberatiA**, **TetzlaffJ**, **AltmanDG**, **GroupTP**. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009:339:b2535.
11. **No authors listed**. Study quality assessment tools. National heart, lung, and blood Institute. https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools (date last accessed 2 December 2020).
12. **Borenstein M**, **Hedges LV**, **Higgins JPT**, **Rothstein HR**. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods*. 2010;1(2):97–111.
13. **DerSimonian R**, **Laird N**. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177–188.
14. **Dayananda KSS**, **Mercer ST**, **Agarwal R**, **Yasin T**, **Trickett RW**. A comparative review of 1,004 orthopaedic trauma patients before and during the COVID-19 pandemic. *Bone Jt Open*. 2020;1(8):568–575.
15. **Mackay ND**, **Wilding CP**, **Langley CR**, **Young J**. The impact of COVID-19 on trauma and orthopaedic patients requiring surgery during the peak of the pandemic: a retrospective cohort study. *Bone Jt Open*. 2020;1(9):520–529.
16. **Konda SR**, **Ranson RA**, **Solasz SJ**, **et al**. Modification of a Validated Risk Stratification Tool to Characterize Geriatric Hip Fracture Outcomes and Optimize Care in a Post-COVID-19 World. *J Orthop Trauma*. 2020;34(9):e317–e324.
17. **Archer JE**, **Kapoor S**, **Piper D**, **Odeh A**. The impact of COVID-19 on 30-day mortality in patients with neck of femur fractures. *Bone Jt Open*. 2020;1(7):326–329.
18. **Fadulelmola A**, **Gregory R**, **Gordon G**, **Smith F**, **Jennings A**. The impact of COVID-19 infection on hip fractures 30-day mortality. *Trauma*. 2020:146040862095135.
19. **Karayiannis PN**, **Roberts V**, **Cassidy R**, **et al**. 30-day mortality following trauma and orthopaedic surgery during the peak of the COVID-19 pandemic. *Bone Jt Open*. 2020;1(7):392–397.
20. **Kayani B**, **Onochie E**, **Patil V**, **et al**. The effects of COVID-19 on perioperative morbidity and mortality in patients with hip fractures. *Bone Joint J*. 2020;102-B(9):1136–1145.
21. **Lazizi M**, **Marusza CJ**, **Sexton SA**, **Middleton RG**. Orthopaedic surgery in a time of COVID-19: Using a low prevalence COVID-19 trauma surgery model to guide a safe return to elective surgery. *Bone Jt Open*. 2020;1(6):229–235.
22. **LeBrun DG**, **Konnaris MA**, **Ghahramani GC**, **et al**. Hip fracture outcomes during the COVID-19 pandemic: early results from New York. *J Orthop Trauma*. 2020;34(8):403–410.
23. **Macey ARM**, **Butler J**, **Martin SC**, **Tan TY**, **Leach WJ**, **Jamal B**. 30-day outcomes in hip fracture patients during the COVID-19 pandemic compared to the preceding year. *Bone Jt Open*. 2020;1(7):415–419.
24. **Malik-TabassumK**, **CrooksM**, **RobertsonA**, **ToC**, **MalingL**, **SelmonG**. Management of hip fractures during the COVID-19 pandemic at a high-volume hip fracture unit in the United Kingdom. *J Orthop*. 2020;20:332–337.
25. **Maniscalco P**, **Poggiali E**, **Quattrini F**, **et al**. Proximal femur fractures in COVID-19 emergency: the experience of two Orthopedics and Traumatology departments in the first eight weeks of the Italian epidemic. *Acta Biomed*. 2020;91(2):89–96.
26. **Mi B**, **Chen L**, **Xiong Y**, **Xue H**, **Zhou W**, **Liu G**. Characteristics and Early Prognosis of COVID-19 Infection in Fracture Patients. *J Bone Joint Surg Am*. 2020;102-A(9):750–758.
27. **Muñoz Vives JM**, **Jornet-Gibert M**, **Cámara-Cabrera J**, **et al**. 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;102-A(13):e69.
28. **Morelli I**, **Luceri F**, **Giorgino R**, **et al**. COVID-19: not a contraindication for surgery in patients with proximal femur fragility fractures. *J Orthop Surg Res*. 2020;15:285.
29. **Muse IO**, **Montilla E**, **Gruson KI**, **Berger J**. Perioperative management of patients with hip fractures and COVID-19: a single institution's early experiences. *J Clin Anesth*. 2020;67:110017.
30. **Narang A**, **Chan G**, **Aframian A**, **et al**. Thirty-day mortality following surgical management of hip fractures during the COVID-19 pandemic: findings from a prospective multi-centre UK study. *Int Orthop*. 2020:1–9.
31. **Rabie H**, **Sharafi MH**, **Oryadi Zanjani L**, **Nabian MH**. Novel Coronavirus Infection in Orthopedic Patients ; Report of Seven Cases. *Arch Bone Jt Surg*. 2020;8(Suppl 1):302–309.
32. **Segarra B**, **Ballesteros Heras N**, **Viadel Ortiz M**, **Ribes-Iborra J**, **Martinez-Macias O**, **Cuesta-Peredo D**. Are hospitals safe? A prospective study on SARS-CoV-2 prevalence and outcome on surgical fracture patients: a closer look at hip fracture patients. *J Orthop Trauma*. 2020;34(10):e371–e376.
33. **Sobti A**, **Memon K**, **Bhaskar RRP**, **Unnithan A**, **Khaleel A**. Outcome of trauma and orthopaedic surgery at a UK District General Hospital during the Covid-19 pandemic. *J Clin Orthop Trauma*. 2020;11(Suppl 4):S442–S445.
34. **Stoneham ACS**, **Apostolides M**, **Bennett PM**, **et al**. Early outcomes of patients undergoing total hip arthroplasty for trauma during COVID-19. *Bone Jt Open*. 2020;1(7):438–442.
35. **Thakrar A**, **Chui K**, **Kapoor A**, **Hambidge J**. Thirty-Day Mortality Rate of Patients With Hip Fractures During the COVID-19 Pandemic: A Single Centre Prospective Study in the United Kingdom. *J Orthop Trauma*. 2020;34(9):e325–e329.

36. **Arafa M**, **Nesar S**, **Abu-Jabeh H**, **Jayme MOR**, **Kalairajah Y**. COVID-19 pandemic and hip fractures: impact and lessons learned. *Bone Jt Open*. 2020;1(9):530–540.
37. **Catellani F**, **Coscione A**, **D'Ambrosi R**, **Usai L**, **Roscitano C**, **Fiorentino G**. Treatment of proximal femoral fragility fractures in patients with COVID-19 during the SARS-CoV-2 outbreak in northern Italy. *J Bone Joint Surg Am*. 2020;102-A(12):e58.
38. **Cheung ZB**, **Forsh DA**. Early outcomes after hip fracture surgery in COVID-19 patients in New York City. *J Orthop*. 2020;21:291–296.
39. **Chui K**, **Thakrar A**, **Shankar S**. Evaluating the efficacy of a two-site ('COVID-19' and 'COVID-19-free') trauma and orthopaedic service for the management of hip fractures during the COVID-19 pandemic in the UK. *Bone Jt Open*. 2020;1(6):190–197.
40. **Clough TM**, **Shah N**, **Divecha H**, **Talwalkar S**. COVID-19 consent and return to elective orthopaedic surgery. *Bone Jt Open*. 2020;1(9):556–561.
41. **De C**, **Wignall A**, **Giannoudis V**, **et al**. Peri-Operative outcomes and predictors of mortality in COVID-19 positive patients with hip fractures: a multicentre study in the UK. *Indian J Orthop*. 2020;54(Suppl 2):1–11.
42. **Egol KA**, **Konda SR**, **Bird ML**, **et al**. Increased Mortality and Major Complications in Hip Fracture Care During the COVID-19 Pandemic: A New York City Perspective. *J Orthop Trauma*. 2020;34(8):395–402.
43. **Lim MA**, **Pranata R**. Coronavirus disease 2019 (COVID-19) markedly increased mortality in patients with hip fracture – A systematic review and meta-analysis. *J Clin Orthop Trauma*. 2020. (Epub ahead of print) PMID: 32958988.
44. **LimMA**. Response to "Letter to the Editor: Coronavirus disease 2019 (COVID-19) markedly increased mortality in patients with hip fracture: A systematic review and meta-analysis". *J Clin Orthop Trauma*. 2020. (Epub ahead of print) PMID: 33204056.
45. **No authors listed**. Coronavirus (COVID-19) Infection Survey. Office for National Statistics. 2020. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/coronaviruscovid19infectionsurveydata (date last accessed 1 November 2020).
46. **Bwire GM**. Coronavirus: Why Men are More Vulnerable to Covid-19 Than Women? *SN Compr Clin Med*. 2020;1:1–3.
47. **George A**, **Stead TS**, **Ganti L**. What's the risk: differentiating risk ratios, odds ratios, and hazard ratios? *Cureus*. 2020;12(8):e10047.
48. **Saklad M**. Grading of patients for surgical procedures. *Anesthesiol*. 1941;2(3):281–284.

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