



# 30-Day Mortality Rate in Hip Fractures Among the Elderly with Coexistent COVID-19 Infection: A Systematic Review

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## Abstract

**Purpose** Hip fractures in the elderly require a multi-disciplinary approach and are associated with increased morbidity and mortality. The current COVID-19 pandemic has affected substantially this high-risk population group. This present review was done to ascertain whether or not the pandemic has affected the 30-day mortality and outcomes of hip fracture in the elderly.

**Research Question** Does the coexistence of COVID-19 infection and hip fractures in the elderly increase the mortality rates?

**Methodology** A systematic review and meta-analysis were conducted using three databases (PubMed, EMBASE and SCOPUS) to compare the mortality rates between COVID-19 positive/suspect and COVID-19 negative patients. The secondary outcomes included comparison of in-hospital mortality, complication rate and length of hospital stay. Risk of bias assessment was done using the MINORS tool.

**Results** The present review included 20 studies. *Primary outcome:* A significantly higher 30 day mortality rate was seen in COVID-19 positive/suspect patients with an Odds ratio of 6.09 (95% CI 4.75–8.59,  $p < 0.00001$ ). *Secondary outcome:* We observed significantly higher rates of inpatient mortality [OR 18.22, (95% CI 7.10–46.75)], complication rate (OR 9.28, 95% CI 4.46–19.30), and length of hospital stay (MD: 4.96, 95% CI 2.86–7.05) in COVID-19 positive/suspect patients as compared to COVID-19 negative patients.

**Conclusion** COVID-19 has deteriorated the outcomes in elderly patients with hip fractures and associated with higher rates of mortality in the short term. A multidisciplinary approach is needed to contain this “pandemic within a pandemic” and improve the overall outcome to survival.

**Keywords** COVID-19 · Novel corona virus · Hip fractures · Proximal femur fractures · 30 day mortality · Elderly

## Introduction

Hip fractures present as one of the commonest injuries in the geriatric population with a reported incidence between 1 and 2% across Europe and the United States of America [1]. Factors related to increased age; osteoporosis, vitamin D deficiency, and multiple systemic comorbidities, make these patients prone to fragility fractures, as well as increase the associated morbidity and mortality [1, 2]. Surgical management is favoured in these patients for early mobilization to prevent repercussions associated with prolonged bed rest; bed sores, deep vein thrombosis or venous thromboembolism and cardiopulmonary insult [3]. The reported rates of 30 day mortality in operated cases vary between 10 and 15% which increases to 15–35% at 1 year of surgery [1, 4].

COVID-19 infection has currently engulfed the world ever since its origin from Wuhan, China in late 2019. With

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high rates of infectivity and transmissibility, the pandemic has been associated with high mortality due to pulmonary complications, especially in the elderly and those associated with systemic co-morbidities like hypertension, diabetes and pre-existent lung diseases [5]. The pandemic required routine patient care and surgeries to be held back, however, the number of trauma and emergency cases including hip fragility fractures have continued to remain more or less similar to pre- COVID-19 era. COVID-19 infection has been shown to increase early mortality (23.8%) in positive patients undergoing major surgeries [6].

With numbers of hip fractures in the elderly increasing and COVID-19 infections multiplying, chances of their co-existence in the same patient is likely, wherein the patient's age and co-morbidities could increase the morbidity and mortality by manifolds when compared to COVID-19 negative patients presenting with such fractures [7, 8].

Fragility hip fractures are a major geriatric burden which require multi discipline collaboration and advanced implants and postoperative rehabilitation. It is already a trauma subset with a high incidence of complications and deaths, and COVID-19 infection has the potential to worsen it. The present review was conceptualised to ascertain the impact of a co-existent infection on the 30-day mortality and inpatient mortality of patients with hip fractures including neck femur, intertrochanteric and subtrochanteric fractures. Additionally, the number of complications and length of hospitalisation were also compared.

## Methodology

### Study Design

This systematic review and meta-analysis were performed in accordance with the PRISMA guidelines [9].

### Search Strategy

The primary electronic search of the literature was conducted on PubMed, Embase and Scopus databases from the date of inception to 4th February 2021 by two authors (RKR and KJ) using a well-defined pre-formulated search strategy (Table 1), without any initial restriction in the language and country of publication. A secondary search of the reference list of the relevant studies identified from the primary search were also done. Finally, a total number of 598 results were obtained.

### Inclusion and Exclusion Criteria

The current review included clinical studies of any design that evaluated at least 10 hip fractures in COVID-19 positive elderly patients and/or compared the same with COVID-19 negative patients, and assessed/compared at least one of the outcomes; 30 day mortality, inpatient mortality, total number of complications and/or length of hospitalization. Exclusion criteria included studies that did not measure the outcomes of interest, included < 10 COVID-19 positive cases, case reports, editorials, review articles, and articles not in the English language.

### Study Selection

All the studies were screened based on their titles and abstracts, independently by three authors (RKR, MSD and SA) and those related to the study question were identified. Subsequently, full texts of all the selected articles were accessed, and relevant studies based on the inclusion/exclusion criteria were included in the current review. Discrepancies between the authors were resolved by mutual agreement.

**Table 1** Search strategy used for the literature search in PubMed, Embase, and Scopus databases

Database	Period-inception to 4th February 2021 with keywords	Results
PubMed	(((((("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields]) OR "ncov"[All Fields]) OR "2019 ncov"[All Fields]) OR "covid 19"[All Fields]) OR "sars cov 2"[All Fields]) OR (("coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date—Publication])) OR (("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields]) OR "coronaviruses"[All Fields])) AND (((("hip fractures"[MeSH Terms] OR "hip"[All Fields] AND "fractures"[All Fields])) OR "hip fractures"[All Fields]) OR ("hip"[All Fields] AND "fracture"[All Fields])) OR "hip fracture"[All Fields])	106
Embase	('covid 19' OR coronavirus) AND hip AND fracture	110
Scopus	( ALL ( covid-19) OR ALL ( coronavirus) AND ALL ( hip AND fracture))	382
Total		598

## Data Extraction

The data extraction was performed by three independent authors (RKR, PK and KJ) from each included article and was entered in a pre-specified data collection excel sheets, mentioning the names of the authors, year of publication, number of COVID-19 positive/suspect and negative patients, relevant demographic parameters, and primary and secondary outcome measures of interest. This was summarized in tabular form (Table 2). All the selected articles were finally reviewed and discussed by all the authors of this study to reduce all possible operator-dependent bias. At the end of this process, 20 publications relevant to this systematic review and meta-analysis at hand were included in this study. Flow chart for the study selection is shown in Fig. 1.

## Outcome Measure

The primary outcomes measure of interest was postoperative mortality at 30 days. The secondary outcomes measure of interest were length of hospital stay, number of complications, and in-patient mortality.

## Statistical Analysis

Meta-analysis was performed if two or more studies reported the outcome of interest of the current review. The random effect model was used and mean difference was calculated for continuous variables and Odds ratio for dichotomous variables. The statistical heterogeneity was determined by using the  $I^2$  test. Reasons for clinical heterogeneity, if any, were also explored. The statistical analysis was done by using Review Manager Software version 5.4 (RevMan 5.4) [10].

## Risk of Bias Assessment

The risk of bias of the included studies was assessed independently by two observers (RKR and VK) using the MINORS tool for the non-randomized studies [11]. The tool consists of 12 items for the comparative studies, and 8 for the non-comparative study, which was adapted for the current review.

## Results

### Search and Screening

The PRISMA flowchart for the study has been presented in Fig. 1. A total of 598 records were identified and full texts were retrieved for 37 studies. Seventeen studies were excluded as per the exclusion criteria and a total of 20 studies [1, 7, 8, 12–28] were included for qualitative analysis.

Comparative meta-analysis was performed from 14 studies [1, 8, 15, 16, 19–28] for 30 days mortality, from 4 studies [8, 16, 17, 22] for in-hospital mortality, and 6 each for the length of hospital stay [1, 8, 15, 17, 25, 28] and number of complications. [1, 8, 14, 18, 22, 26]

## Characteristics of the Studies

A summary of the studies included in the review has been presented in Table 2. Of the 20 studies, 16 were retrospective [1, 7, 13–18, 21–28] and 4 were prospective [8, 12, 19, 20] studies. Nine studies were multicentric trials [1, 7, 15, 17, 19, 21, 23, 25, 28]. A total of 3211 patients were included in the review; of these, the pooled analysis was done for 3157 patients in 18 studies [1, 7, 8, 14–28]. The mean age of patients was 81.79 years with a range from 71.9 to 86.5 years. The review included 925 males and 2028 females reported in 18 studies [1, 7, 8, 12–15, 17–26, 28] and the mean length of hospital stay ranged from  $5 \pm 2.6$  to 24.21 days.

## Assessment of Risk of Bias

The overall risk of bias was assessed as low for the included studies as depicted in Figs. 2, 3. There were 15 nonrandomized comparative study [1, 8, 15–20, 22–28] and rest 5 [7, 12–14, 21] were observational studies/case series. MINORS tool Score was  $\geq 19$  for 13 nonrandomized comparative studies [1, 8, 15–17, 19, 22–28] while  $\geq 12$  for all 5 noncomparative studies [7, 12–14, 21].

## Results of Meta-Analysis Between COVID-19 Positive/Suspects Versus COVID-19 Negative Patients

### Primary Outcome

30-days mortality rates: This was compared between the 2 groups in 14 studies [1, 8, 15, 16, 19–28] and showed a significantly high mortality rate in COVID-19 positive/suspect patients with an Odds ratio of 6.09 (95% CI 4.75, 7.81,  $p < 0.00001$ ) (Fig. 4).

### Secondary Outcomes

**In-patient Mortality** Comparative meta-analysis in 4 studies [8, 16, 17, 22] revealed significantly higher in-hospital mortality rates in COVID-19 positive/suspect patients with an Odds ratio of 18.22 (95% CI 7.10, 46.75,  $p < 0.00001$ ) (Fig. 5).

**Number of Complications** The rate of complications like infections, acute renal failure, deep vein thrombosis, myo-

**Table 2** Demography, pre-, and postoperative parameters of included studies

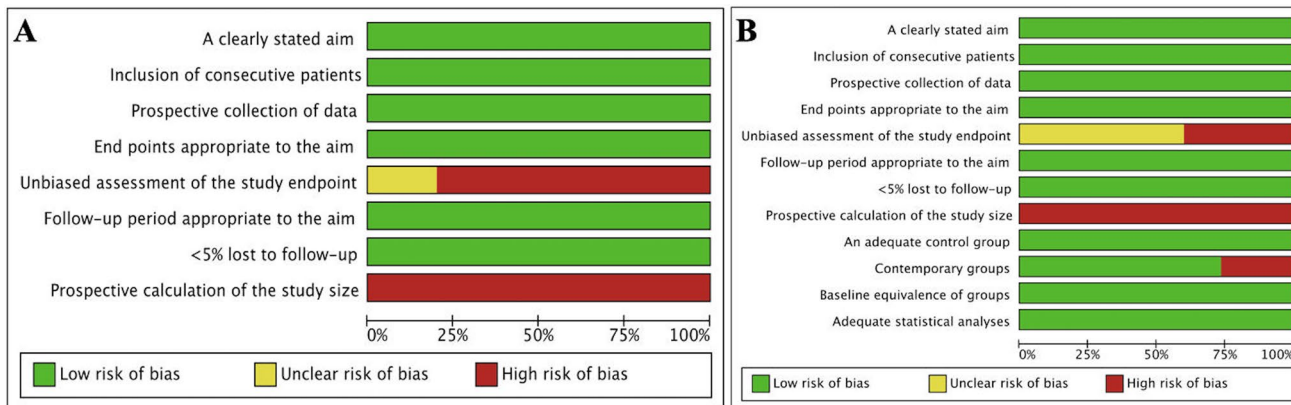
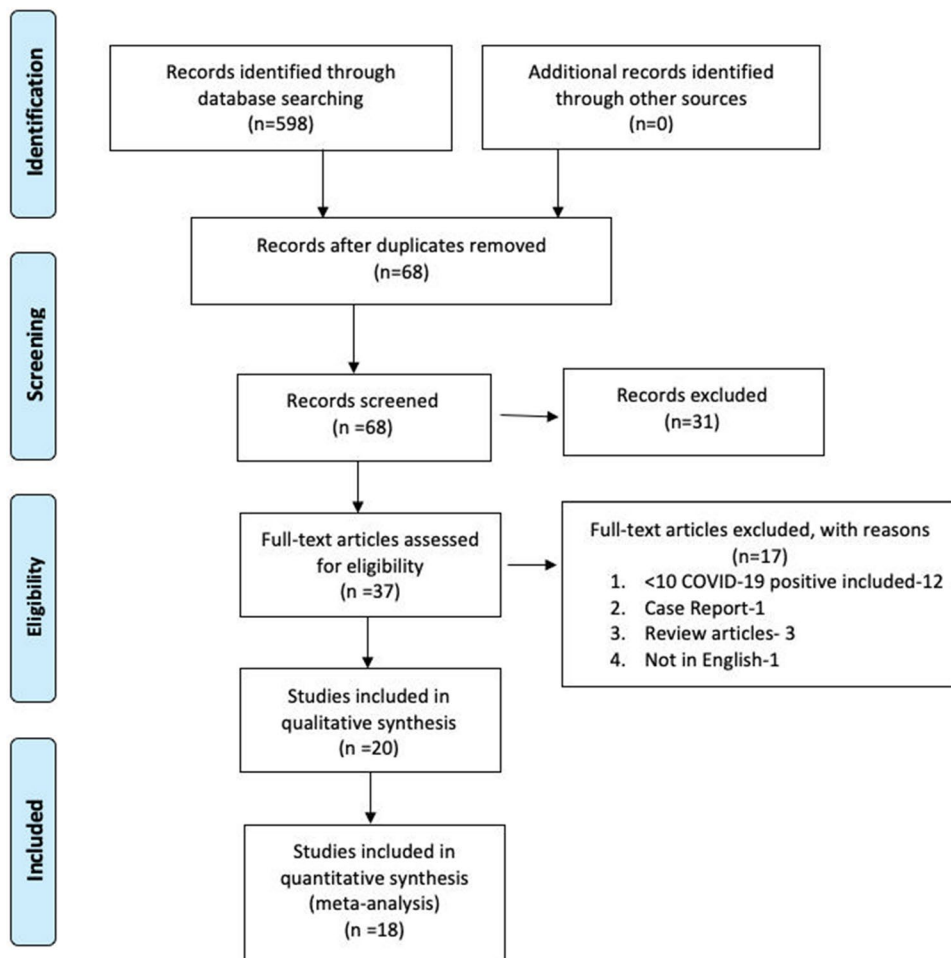
Sl no	Author/Year	Type of study	Number of hips			Mean age (years) (SD)	Gender (M/F)	Non operative cases	Mean LOS (days) (SD)	No. of complications	In patient mortality	30 day mortality
			CP	CS	CN							
1	Catellani et al. 2020 [12]	Prospective study	16	-	-	84.3	10/6	3		Pre-op:3 Post op:4	-	
2	Cheung et al. 2020 [13]	Retrospective study	10	-	-	79.7 ± 5.75	2/8	0	7.8	5	1 on Post-operative day 19	
3	Egol et al. 2020 [8]	Prospective study	17	14	107	CP:82.4 CS:80.6 CN:83.4	CP-12/5 CS-4/10 CN-34/73	CP-4 CS-0 CN-0	CP-9.8 ± 5.2 CS-7 ± 5.9 CN-5 ± 2.6	CP-13 CS-7 CN-8	CP-9 CS-2 CN-6	
4	Fadulemola et al. 2020 [14]	Retrospective study	20	-	55	CP-83.7 CN-83.5	CP-7/13 CN-15/40	CP-1 CN-2	-	CP-1 CN-1	CP-10 CN-4	
5	Hall et al. 2020 [15]	Retrospective study	27	-	290	CP-83.6 ± 11.3 CN-80.4 ± 10.6	Overall-106/211	CP-02 CN-12	CP-11.3 ± 7.5 CN-7.8 ± 4.6	-	CP-9 CN-24	
6	Kayani et al. 2020 [1]	Retrospective study	82	-	340	CP-71.9 ± 9.5 CN-72.7 ± 6.7	CP-31/51 CN-136/204	CP-0 CN-0	CP-13.8 ± 4.6 CN-6.7 ± 2.5	CP-73 CN-119	CP-25 CN-35	
7	Konda et al. 2020 [16]	Retrospective study	17	14	105	CP/CS:81.6	-	-	CP/CS:8.9 ± 6.8	CP/CS:72 CN: 1	CP/CS:11 CN: 6	
8	LeBrun et al. 2020 [17]	Retrospective study	10	-	50	CP-86.5 ± 7.9 CN-84.7 ± 7.5	CP-3/6 CN-12/38	CP-02 CN-0	CP-8 ± 2.25 CN-6 ± 1.75	CP/CN-18 CN-1	-	
9	Maniscalco et al. 2020 [18]	Retrospective study	32	-	89	Overall 81.75 ± 9.74	Overall-32/89	0	-	CP-14 CN-4	CP-9+5 CN-2+1	
10	Narang et al. 2020 [19]	Prospective study	86	-	596	CP-86 CN-83	CP-32/ 54 CN-170/ 426	-	-	-	CP-30/86 CN-36/596	
11	Thakrar et al. 2020 [20]	Prospective study	12	-	31	Overall 81.6 ± 11.3	Overall-23/20	CP-0 CN-0	Clinical frailty score-4.6 ± 1.5	-	CP-4 CN-7 Not tested-2	
12	Vives et al. 2020 [21]	Retrospective study	23	-	113	Overall-85 ± 9	Overall-34/102	12	-	-	CP-7 CN-4 Not tested-2	
13	De et al. 2020 [7]	Retrospective case series	34	-	-	Over all 85.9 (SD 7.7)	Overall-12/ 22	1	22.4 (SD 11.8)- mortality group	16	CP-14	
14	Arafa et al. 2020 [22]	Retrospective study	19	-	78	CP- 86.21 (SD 7.71) CN- 83.05 (SD 7.64)	CP-9/10 CN-21/57	2	CP-24.21 (SD 19.29) significantly higher than CN	CP-7 CN-7	CP-7 CN-9	
15	Karayannis et al. 2020 [23]	Retrospective study	21	-	182	Overall- 81.3 (SD-9.7)	Overall-65/138	0	-	CP-2	CP-4 CN-3	

**Table 2** (continued)

Sl no	Author/Year	Type of study	Number of hips			Mean age (years) (SD)	Gender (M/F)	Non operative cases	Mean LOS (days) (SD)	No. of complications	In patient mortality	30 day mortality
			CP	CS	CN							
16	Macey et al. 2020 [24]	Retrospective study	10	-	66	Overall Median (IQR) 83 (73–87)	Overall-58/18	3	Median 11.5 (6–22)	Overall 21	-	CP-2 CN-9
17	Rasidovic et al. 2020 [25]	Retrospective study	114	-	290	CP-85.16 (SD 8.67) CN-82.88 (SD 8.59)	CP-43/71 CN-80/210	CP-5 CN-5	CP-17.66 (SD 11.16) CN-12.04 (SD 7.17)	-	-	CP-37 CN-21
18	Ward et al. 2020 [26]	Retrospective study	46	-	86	CP-83.4±9.8 CN-81.4±10.7	CP-12/34 CN-24/62	CP-1 CN-4	Median CP-21.5 (1–75) CN-10 (2–67)	CP-23 CN-20	-	CP-17 CN-9
19	Mamarelis et al. 2020 [27]	Retrospective study	11	-	26 (and 4 not tested)	-	-	CP-3 CN-3	-	-	-	CP-6 CN-2
20	Wright et al. 2021 [28]	Retrospective study	17	-	51	Overall-81.1 (±11.35)	Overall-18/50	CP-1 CN-1	CP-17 (SD 5.6, range 8–27) CN-10 (SD 8.7, range 1–53)	-	-	CP-5 CN-3

CP: COVID-19 Positive; CS: COVID-19 Suspect; CN: COVID-19 Negative; LOS: Length of Stay, M: male, F: female; SD: Standard deviation; IQR: Interquartile

**Fig. 1** PRISMA flow diagram for the study selection



**Fig. 2** Risk of bias graph for **a** non-comparative studies **b** comparative studies

cardial infarction and acute respiratory failure, was compared between the 2 groups in 6 studies [1, 8, 14, 18, 22, 26] and the number of complications was found to be significantly high in COVID-19 positive/suspected patients with an Odds ratio of 9.28 (95% CI 4.46, 19.30;  $p < 0.00001$ ) (Fig. 6).

**Length of Hospital Stay** It was compared between the 2 groups in 6 studies [1, 8, 15, 17, 25, 28] and showed that the length of hospital stay was significantly higher in COVID-19 positive patients as compared to COVID-19 negative patients, with a mean difference of 4.96 days (95% CI 2.86, 7.05;  $p < 0.00001$ ) (Fig. 7).

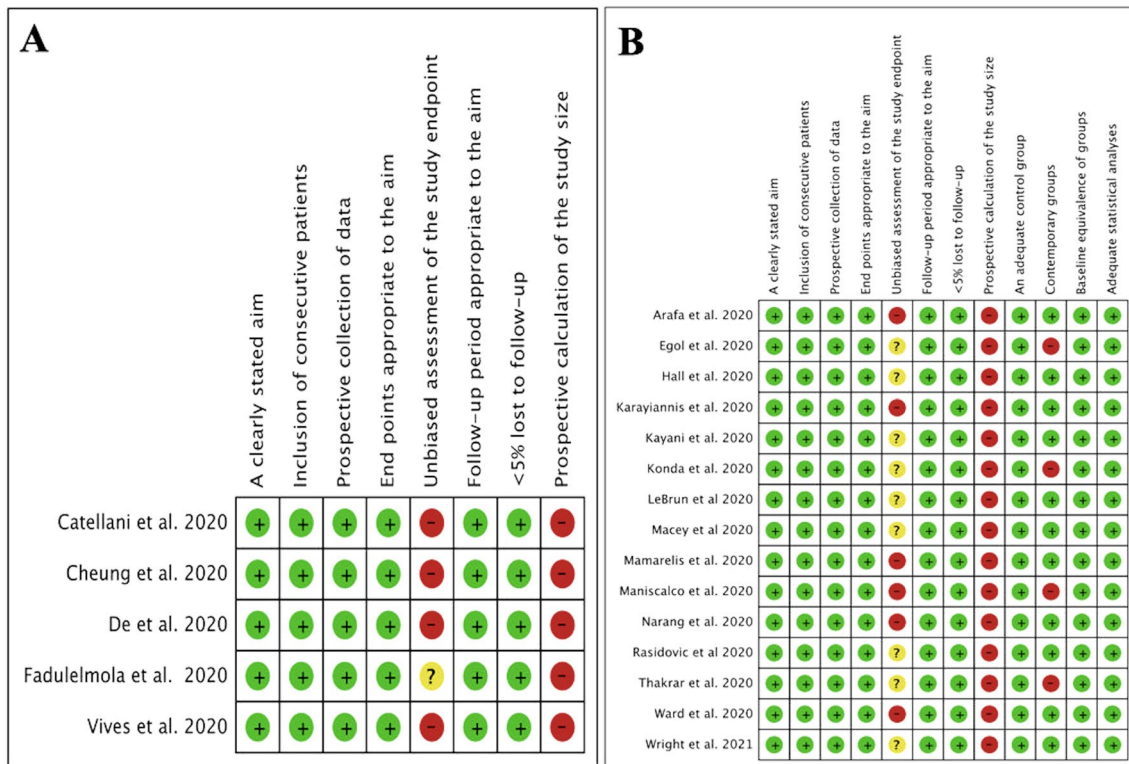


Fig. 3 Risk of bias summary for a non-comparative studies b comparative studies

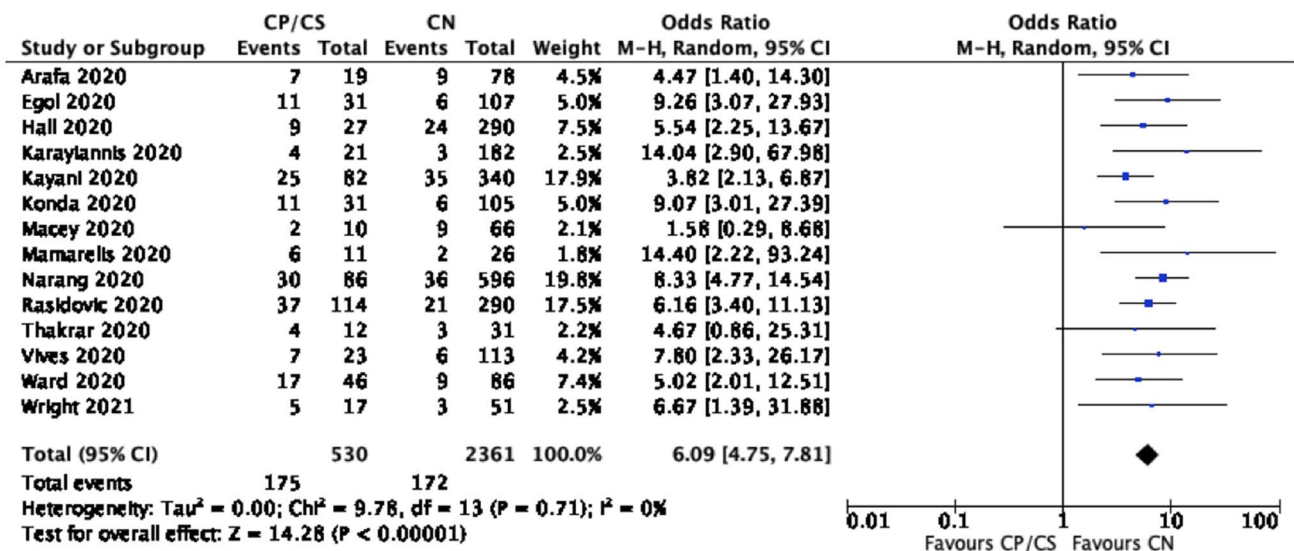


Fig. 4 Comparison of 30 day mortality

**Pooled Analysis**

Pooled analysis was done from 17 studies [1, 8, 14–28] for analysing the rates of COVID-19 positive/suspect patients in

hip fractures in the elderly. We observed a rate of 19.2%; the heterogeneity for this event was high ( $I^2 = 88.98\%$ ) (Fig. 8).

We also pooled the data for overall mortality in these 626 COVID-19 positive/suspect patients from 18 studies [1, 7, 8, 14–28] and found a mortality rate of 34.7%, the heterogeneity for this event was low ( $I^2 = 0$ ) (Fig. 9).

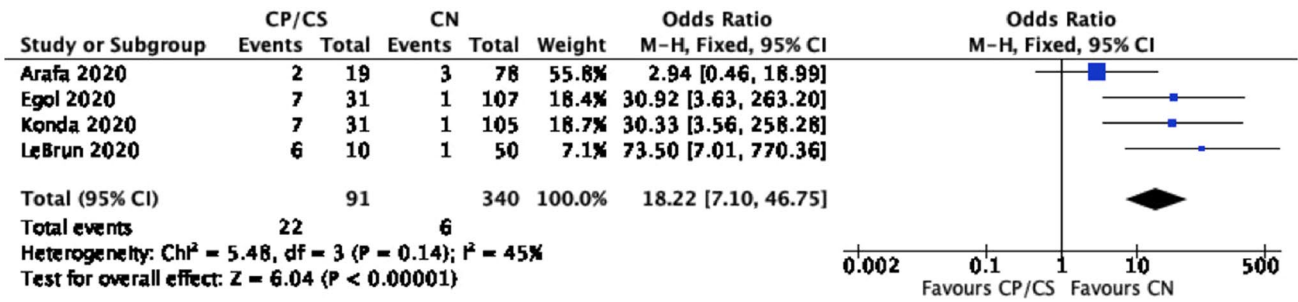


Fig. 5 Comparison of in-hospital mortality

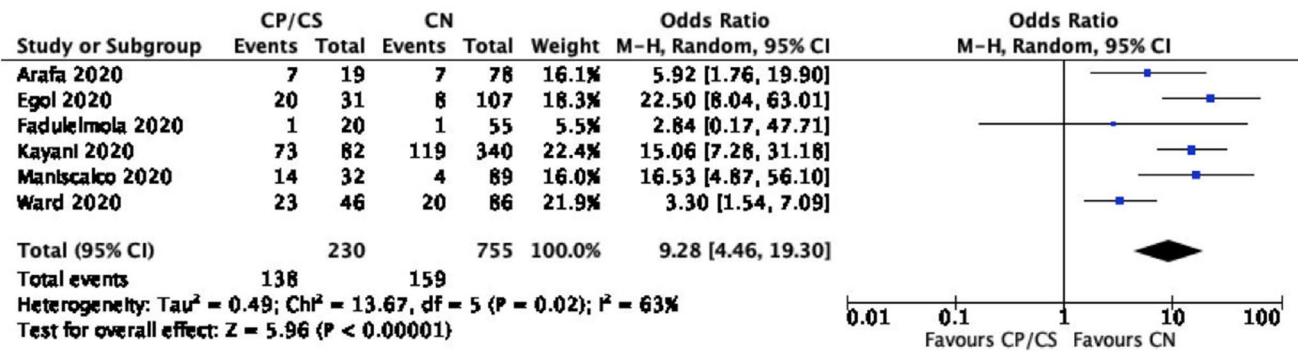


Fig. 6 Comparison of complication rate

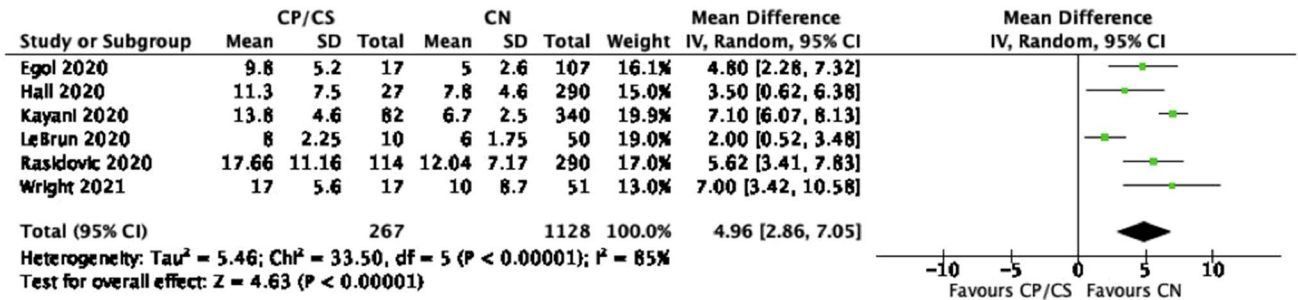


Fig. 7 Comparison of length of hospital stay

### Discussion

Hip fractures in the elderly are a major group of trauma wherein associated disabilities are significant; prolonged bed riddance and need of mobilizing aids with geriatric care facilities [29]. Over and above this these injuries witness a high rate of early mortality, with reported rate of 30 day mortality being 7–15% [1, 4, 30]. The probable reason for such high rates of death in these patients is the associated acute inflammatory over-activation (increased markers like Interleukins-6,8 and 1; Tumour necrosis factor-alpha and C reactive proteins) resulting in aberrant

hyper-coagulability (increased platelet reactivity and Factor VIII) with increased physiological stress (increased cortisol and catecholamines); these induce pulmonary and vascular complications, i.e. myocardial infarction, embolism, stroke etc. [31–33]. This is amplified by the already existing preconditions like hypertension, diabetes, and other cardiorespiratory diseases in this subset of elderly trauma patients [34].

In turn, the COVID-19 infection has also been shown to be resulting in an inflammatory cascade involving what is known as “cytokine storm”, which results from macrophages and neutrophils entering the lung tissue [35]. This deteriorates the prognosis by causing acute respiratory distress



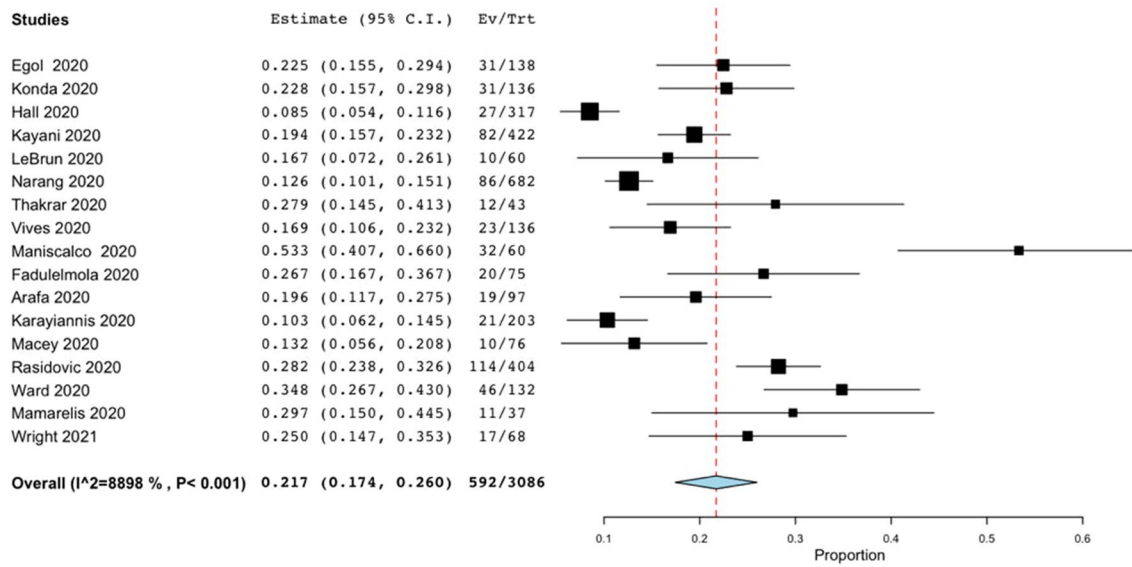


Fig. 8 Pooled analysis for COVID-19 positive plus COVID-19 suspect patients with hip fractures

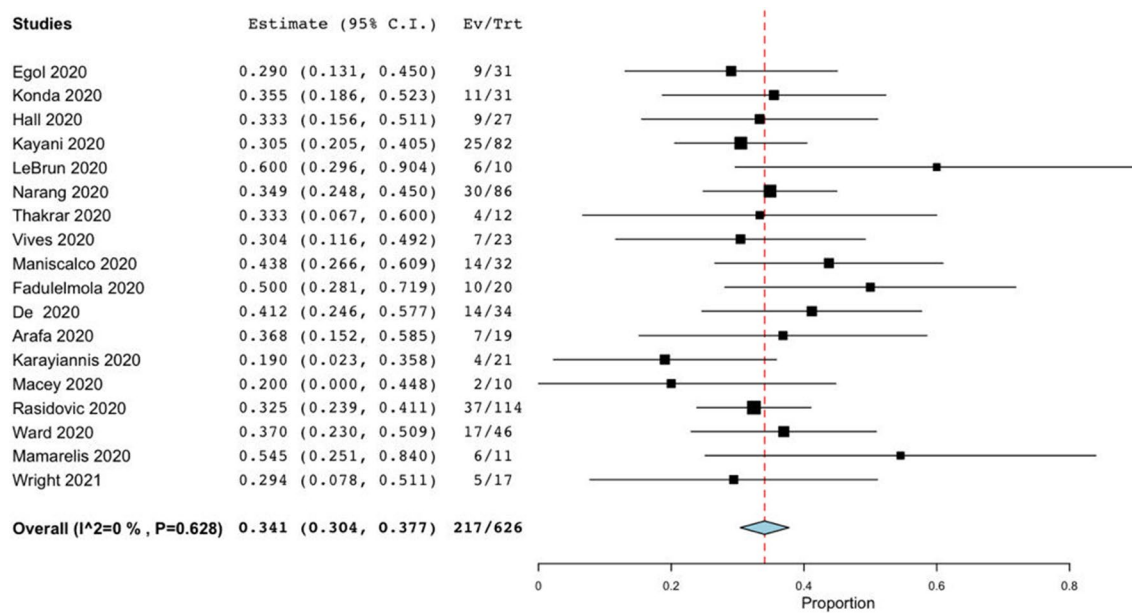


Fig. 9 Pooled analysis for mortality in COVID-19 positive patients with hip fractures

syndrome (ARDS), leading to increased mortality [35, 36]. Besides this, the co-morbidities have been shown to be independent high-risk factors of worsened outcomes of COVID-19 infections [5].

Thus, in a nutshell both COVID-19 infection and hip fragility fractures could exhibit similar pro-inflammatory pathogenesis, which could lead to devastating outcomes in patients having both pathologies. Older patients are prone to infections and COVID-19 has been shown to demonstrate extreme infectivity and pathogenicity [37]. In terms of

overall numbers of COVID-19 infected/suspected elderlies presenting with fragility hip fractures, our pooled analysis across 17 studies showed a positivity rate of 19.2%, which is extremely high and possibly depicts a “pandemic within a pandemic” scenario.

The present review has also shown increased rates of mortality in these infected patients. Our results showed that the rate of 30 day mortality in these patients across 18 studies, was 34.7%, which is 3.5 times the normally reported mortality in patients of hip fractures in the

pre- COVID-19 era [1, 4, 30]. The 1 year mortality in the pre- COVID-19 times had been reported to be between 20 and 35% [1, 4, 29]. These rates convey a very dark picture, wherein the patients with both the pathologies have reported a massive surge in early 1 month mortality, which is even more than what used to be at 1 year earlier.

During the pandemic itself when we compared 30-day mortality between patients with hip fractures, who were negative for COVID-19 infection and those who were either positive or suspected, the results showed a significantly lower mortality rate in COVID-19 negative patients. The total number of deaths in the COVID-19 negative patients was 172/2361, whereas the number of deaths in the other group was 175/530 patients. Interestingly, since the pandemic is on only for a year, the published literature have not shown mortality rates at 1 year or longer periods of time, which could be devastatingly high on longer follow ups, presenting an even gloomier picture.

Another important aspect in these patients is the frequency of complications like deep infections, acute renal failure, thromboembolism, and myocardial infarction, etc. The review showed that these numbers are significantly higher in the COVID-19 positive/suspect group (138/230 cases) compared to COVID-19 negative patients (159/755), which may be related to the overall pathogenesis of the co-existent infection and the fracture, as discussed above. Some of these complications are life-threatening and could be the probable events leading to increased deaths, which can be during hospitalisation itself or subsequently thereafter.

With more number of complications, the duration of hospitalisation also increases and our results confirm the same, wherein it was significantly longer in infected patients, which could lead to more nosocomial complications, leading to a vicious cycle increasing the number of deaths.

Looking into mortality during index hospitalisation, the meta-analysis of 4 studies comparing these rates between the groups, showed that in-hospital mortality is also extremely high in patients with both the infection and hip fractures. 22/91 patients died in this group whereas deaths in the negative group were only 6/340.

The extreme differences in mortality rates in the present review between the groups, clearly suggest that extra optimization and care are needed in this subset of patients who are anyways at increased risk of early mortality, which can be further compounded by the co-existent COVID-19 infection. One of the limitations of the present review is the relative delay in surgeries in some COVID-19 positive/suspected patients compared to the COVID-19 negative groups in some included studies [27, 28], for preoperative optimization of the patients, which itself may have an effect on overall outcomes and mortality as delaying hip surgeries have been documented to cause inferior outcomes.

Fragility hip fractures are widely considered as an economic burden in view of associated morbidity in the patients and associated costs of geriatric care; superimposed COVID-19 infection worsens the outcomes further and could increase this burden manifold [38]. The present review highlighted the compounded issue with this specific subset of elderly trauma patients in the era of COVID-19 pandemic. A coexistent infection in an already vulnerable group of patients is associated with an exponential increase in the number of complications and deaths. A multidisciplinary approach is needed from the health care providers to contain this “pandemic within a pandemic” and improve the overall outcomes.

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## Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical standard statement** This article does not contain any studies with human or animal subjects performed by any of the authors.

**Informed consent** For this type of study informed consent is not required.

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