Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Perioperative mortality and morbidity of hip fractures among COVID-19 infected and non-infected patients: A systematic review and meta-analysis

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ABSTRACT

Purpose: Hip fractures among elderly patients are surgical emergencies. During COVID-19 pandemic time, many such patients could not be operated at early time because of the limitation of the medical resources, the risk of infection and redirection of medical attention to a severe infective health problem.
Methods: A search of electronic databases (PubMed, Medline, CINAHL, EMBASE and the Cochrane Central Register of Controlled Trials) with the keywords "COVID", "COVID-19", "SARS-COV-2", "Corona", "pandemic", "hip fracture", "trochanteric fracture" and "neck femur fracture" revealed 64 studies evaluating treatment of hip fracture in elderly patients during COVID-19 pandemic time. The 30-day mortality rate, inpatient mortality rate, critical care/special care need, readmission rate and complications rate in both groups were evaluated. Data were analyzed using Review Manager (RevMan) V.5.3.
Results: After screening, 7 studies were identified that described the mortality and morbidity in hip fractures in both COVID-19 infected (COVID-19 +) and non-infected (COVID-19 −) patients. There were significantly increased risks of 30-day mortality (32.23% COVID-19 + death *vs.* 8.85% COVID-19 − death) and inpatient mortality (29.33% *vs.* 2.62%) among COVID-19 + patients with odds ratio (*OR*) of 4.84 (95% *CI*: 3.13−7.47, $p < 0.00001$) and 15.12 (95% *CI*: 6.12−37.37, $p < 0.00001$), respectively. The COVID-19 + patients needed more critical care admission (*OR* = 5.08, 95% *CI*: 1.49−17.30, $p < 0.009$) and they remain admitted for a longer time in hospital (MD = 3.6, 95% *CI*: 1.74−5.45, $p = 0.0001$); but there was no difference in readmission rate between these 2 groups. The risks of overall complications (*OR* = 17.22), development of pneumonia (*OR* = 22.25), and acute respiratory distress syndrome/acute respiratory failure (*OR* = 32.96) were significantly high among COVID-19 + patients compared to COVID-19 − patients.
Conclusions: There are increased risks of the 30-day mortality, inpatient mortality and critical care admission among hip fracture patients who are COVID-19 +. The chances of developing pneumonia and acute respiratory failure are more in COVID-19 + patients than in COVID-19 – patients.

Introduction

The COVID-19 has spread to more than 210 countries and affected 155,665,214 people worldwide, including 3,250,648 deaths as of 6th May 2021.[1] Because of the highly infectious nature of the disease and increased mortality rate among the elderly and immunocompromised patients, the World Health Organization has declared COVID-19 as a massive global pandemic and a significant public health problem.[1] In order to contain the spread of the disease and to accommodate such a vast patient pool of COVID-19, the healthcare resources were combined, and it was redirected to prioritize medical emergencies and COVID-19 treatment over non-emergency medical and surgical conditions.[2–5]

Hip fractures are surgical emergencies. Most of these patients are elderly individuals with numerous comorbidities.[6–10] They

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usually develop this fracture after a trivial fall at home because of poor bone quality and neurological disorders. Consequently, the incidence of hip fracture has remained stably high even during the period of the COVID-19 pandemic.[11–13] Management of such fractures in these vulnerable immunocompromised patients is a big challenge.[11–13] There have been numerous advancements in the management of geriatric hip fractures, including better perioperative patient care, multidisciplinary approach, better implant, cementation procedures, fluid and antibiotic protocols and rehabilitation measures. Despite that, 9%–13% of patients die within 30-day, and 14%–36% die within 1 year following hip fracture surgery.[14,15] Besides, the functional outcome, quality of life, and return to preinjury activity level among the survivors are poor.[14,15] Amidst the COVID-19 pandemic, when the entire medical attention is diverted towards COVID-19 management, delaying of hip fracture surgery might cause increased complication and perioperative mortality. Again, symptomatic infection with COVID-19 in the hip fracture patients might cause a delay in surgery, increased length of hospital stay, increased need for ventilator support, and increased chances of respiratory complications and mortality.[16–25]

A collaborative international study group reported 23.8% mortality among COVID-19 infected (COVID-19 +) patients ($n = 1128$) who underwent surgery. The mortality rate was even higher in emergency surgery (25.6%) and orthopaedic procedures (28.8%).[26] Many authors reported a higher 30-day mortality rate in hip fractures among COVID-19 + patients compared with COVID-19 non-infected (COVID-19 −) patients.[18–22] Nevertheless, a few researchers did not observe a significant difference regarding mortality between these 2 groups of patients.[24] Several cohort studies reported no significant difference in time to surgery, type of treatment, complications, and 30-day mortality of hip fracture patients admitted during the COVID-19 pandemic when compared to the pre-pandemic period.[12,19,27,28] Therefore, this systematic review and meta-analysis was conducted to evaluate the 30-day mortality and complications in COVID-19 + and COVID-19 − patients with hip fractures.

Methods

This systematic review/meta-analysis was performed following preferred reporting items for systematic reviews and meta-analyses statement standards.[29] It has been registered in PROSPERO. The registration number is CRD42020200592.

Literature search strategy

A literature search was performed on 25th July 2020 by 2 authors (Varghese P, Panigrahi S) to identify studies on hip fractures during COVID-19 pandemic. The electronic databases of PubMed, Medline, CINAHL, EMBASE and the Cochrane Central Register of Controlled Trials were searched using the keywords “COVID”, “COVID-19″, “SARS-COV-2”, “Corona”, “pandemic”, “hip fracture”, “trochanteric fracture” and “neck femur fracture”. The search was limited to the English literature and human being. The title and abstract of retrieved articles were assessed carefully for possible inclusion in this review. The full text was assessed when the title and abstract were inconclusive. A manual search of the articles from the bibliography and book chapter was also performed to get more studies related to the topic. We resolved any discrepancies in study selection by a discussion between the authors. The third author (Tripathy SK) was consulted in the event of disagreement.

Study selection

The inclusion criteria for this systematic review were as follows: (1) the study design must be a randomized-controlled trial or a cohort study; (2) the study must evaluate the mortality and morbidity of hip fracture surgery in both COVID-19 + and COVID-19 − patients; (3) the study must have recruited patients of any gender above the age of 18 years.

Studies on open fractures or pathological fractures were not considered. Similarly, studies reporting the mortality and morbidity of hip fractures in only COVID-19 + patients were excluded.

The hip fractures in this review included both intracapsular (neck femur fractures) and extracapsular fractures (intertrochanteric and subtrochanteric fractures). Patients with clinical symptoms/signs of COVID-19 with positive nose or throat swab (assay with reverse transcriptase-polymerase chain reaction (RT-PCR)) for 2019-nCoV were classified as "COVID-19 +". Patients were classified as “COVID-19 −” if they were asymptomatic and the throat and nose swabs assays were negative for 2019-nCoV using RT-PCR. Patients who were clinically symptomatic with a high grade of suspicion but the swab tests were negative, were labelled as “COVID-19 suspect”. For quantitative analysis of data, all “COVID-19 suspect” patients were included in the COVID-19 + group and “COVID-19 not tested” patients were considered as COVID-19 − group.

Data extraction

Two authors (Tripathy SK, Varghese P) extracted data from the included studies. The details (authors, year of publication, study design, demographic properties, surgical details, follow-up, 30-day mortality, the need of intensive care unit (ICU) care, readmission and complications) were filled up in standardized forms. Any disagreement was resolved through the discussion with the third author (Sen RK).

The primary objective of this study was 30-day mortality rate in both COVID-19 + and COVID-19 − patients. The secondary objectives were inpatient mortality rate, need of critical care/special care (ICU/high dependency unit (HDU)/step down unit), readmission rate and complication rate in both groups of patients.

Methodological quality and risk of bias assessment

The methodological quality and risk of bias of the studies were assessed by the Newcastle–Ottawa scale (NOS) by 2 authors (Tripathy SK and Varghese P).[30] The NOS uses a star system with a maximum of 9 stars to evaluate a study in 3 domains (8 items): the selection of the study groups, the comparability of the groups, and the ascertainment of the outcome of interest. Each item was allocated 1 star for low risk and no star for high risk. Studies that received a score of 9 stars were considered as low risk of bias, 7 or 8 stars as moderate risk, and 6 or less as high risk of bias.[30] Any disagreements were resolved by discussion between 2 authors. If no agreement could be reached, the opinion of the third author (Sen RK) was sought.

Statistical analysis

Data were analyzed using Review Manager (RevMan) V.5.3. The data were pooled and expressed as mean difference (MD) with 95% *CI* for continuous data. The *OR* and 95% *CI* were evaluated for dichotomous outcomes. A $p < 0.05$ was considered as statistically significant. The heterogeneity among the cohort studies was assessed by Cochrane's Q ($\chi 2$, $p < 0.10$) and quantified by I^2.[31]

I^2>50% and $p < 0.10$ were considered as a threshold of significant heterogeneity.[32–34] The random-effects model was applied to address the high degree of heterogeneity.[32–34]

Results

Study identification, study quality, risk of bias and patient demographics of the included studies

Searches of electronic databases and other sources retrieved 64 studies, of which 7 studies were eligible for review after screening (**Fig. 1**).[16,18–21,24,35] There were 2 prospective studies[19,24] and 5 retrospective comparative studies.[16,18,20,21,35] The inclusion and exclusion criteria were well defined in all studies. Assessment of quality of the studies using NOS revealed a low risk of bias in 1 study, moderate risk of bias in 5 studies and a high risk of bias in 1 study. A total of 1162 hip fracture patients were treated during the COVID-19 pandemic. There were 196 COVID-19 + patients and 966 COVID-19 − patients (**Table 1**). The mean age of patients in all studies was above 70 years. Regarding gender distribution, there were 423 male patients and 739 female patients (**Table 1**). The body mass index (BMI) was reported in 3 studies, and the average BMI was <30 kg/m^2. Regarding domicile status, 3 studies (n = 797) mentioned in details. These studies mentioned whether the patients were staying independently at home or in groups/clusters such as a package of care, nursing home or residential home.[18,21,35] Ninety-two of 118 COVID-19 + patients and 357 of 679 COVID-19 − patients stayed in clusters/groups; this difference was statistically not significant (MD = 3.45, p = 0.09) (**Table 1**).

Preoperative comorbidities

Three studies[18,20,35] reported the preoperative comorbidities among the COVID-19 + and COVID-19 − patients with regards to their cardiovascular disease status, lungs diseases, diabetes mellitus, hypertension, renal failure, neurological problems and immunocompromised conditions, including malignancy (**Table 2**). The comorbidities and functional status among the hip fractured patients that predict the mortality were better indicated by numerous comorbidity indices such as Charlson comorbidity index, clinical frailty scale and Nottingham hip fracture scores (**Table 2**). Comparison of these scores has been reported in 6 studies.[18–21,24,35] However pooled analysis of 4 studies[18,20,21,35] (n = 936) was possible and it did not show a significant difference between COVID-19 + and COVID-19 − patients (standard MD = 0.16, 95% *CI*: −0.21–0.54, p = 0.39) (**Fig. 2**). Nevertheless, there was a significant difference between these 2 groups of patients in terms of the smoking habit. There were significantly increased numbers of smokers (current and former) amongst the COVID-19 + patients (51/116 *vs.* 128/495; *OR* = 2.30, 95% *CI*: 1.50–3.51, p = 0.0001).

Surgery details of the included studies

Surgical fixation or partial/total arthroplasty is a choice of treatment for hip fractures among elderly patients (**Table 1**). Non-operative treatment is usually reserved for severely medically ill patients. Four studies mentioned non-operative treatment. Pooled data of 3 studies[18,21,35] (n = 514), where the surgical procedures were reported separately for COVID-19 + and COVID-19 − patients,

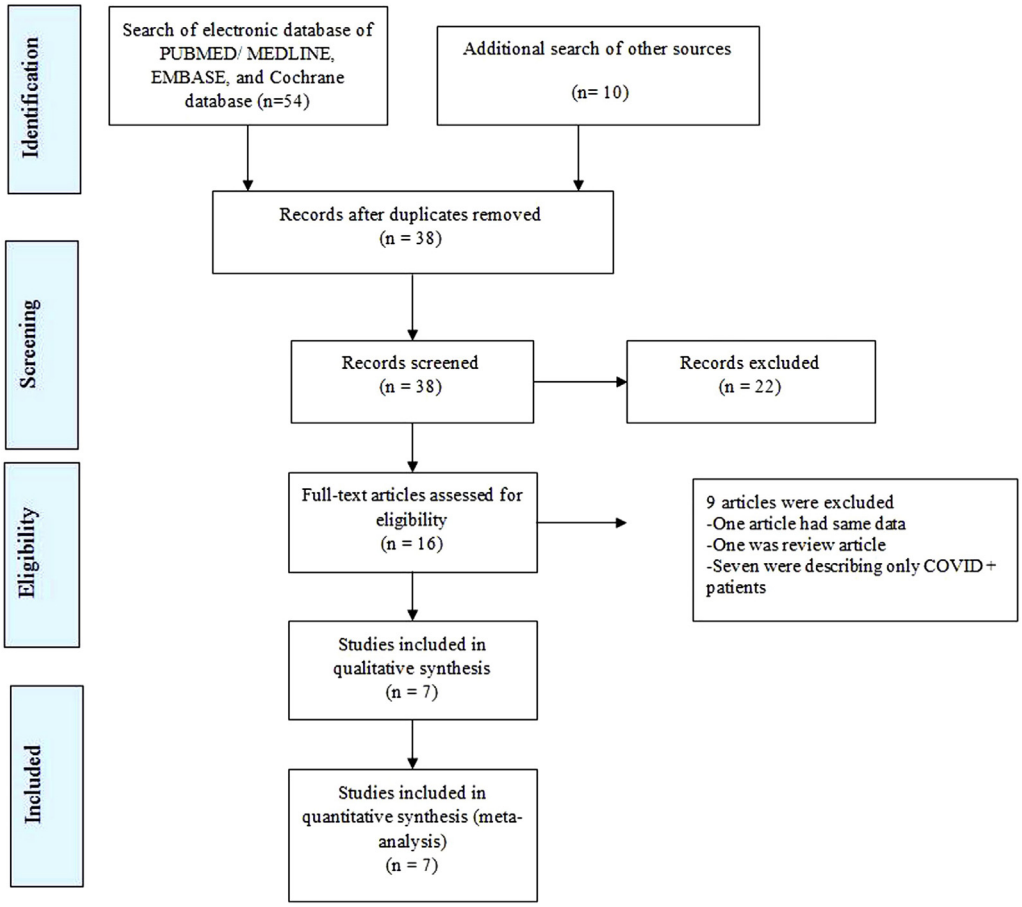

Fig. 1. PRISMA flow diagram showing methods of study recruitment.

Table 1
Demographic properties, fracture type and surgical techniques as described in the included studies.

Study (country)	Vives et al.[16] (Spain)	Kayani et al.[18] (UK)	Thakrar et al.[19](UK)	Egol et al.[20] (USA) (COVID + & COVID suspect* vs. COVID −)	Hall et al.[21] (UK)	Chui et al.[24] (UK)	LeBrun et al.[35] (USA)
Study design	Multicentre, retrospective cohort study	Multicentre retrospective cohort study	Prospective cohort study	Multiple-hospital retrospective study	Multicentre retrospective cohort study	Prospective cohort study	Multicentre retrospective cohort study.
Quality of the study (NOS)#	7	9	7	8	8	6	8
Sample size, *n*							
COVID +	23	82	12	31 (17/14*)	27	12	9
COVID −	113	340	31	107	290	35	50
Age (years)							
COVID +	85.3 ± 7.6	71.9 ± 9.5	81.6 ± 11.3	82.4 ± 9.6/80.6 ± 9.9*	83.6 ± 11.3	86.8 ± 6.4	86.5 ± 7.9
COVID −		72.7 ± 6.7		83.4 ± 10.4	80.4 ± 10.6	78.5 ± 13.3	84.7 ± 7.5
Sex (male:female)							
COVID +	34:102	31:51	23:20	12:5/4:10	14:13	5:7	3:6
COVID −		136:204		34:73	92:198	23:12	12:38
BMI (kg/m^2)							
COVID +	NM	25.8 ± 3.2	NM	25.5 ± 8.0/23.8 ± 4.1*	NM	NM	21.4 ± 4.5
COVID −	NM	25.1 ± 2.5	NM	24.3 ± 4.6	NM	NM	22.9 ± 4.1
Domicile status, *n* (%)							
COVID +	Nursing home: 30 (22.1) Family home: 106 (77.9)	Independent: 2 (2.4) Package care: 15 (18.3) Residential home:39 (47.6) Nursing home: 26 (31.7)	NM	NM	Home: 19 (70.4) Package care/nursing home: 6 (22.2) Hospital: 2 (7.4)	NM	Home: 5 (55.6) Nursing home: 2 (22.2) Assisted living facility: 2 (22.2)
COVID −		Independent: 69 (20.3) Package care: 215 (63.2) Residential home: 43 (12.7) Nursing home: 13 (3.8)	NM	NM	Home: 211 (72.8) Care/nursing home: 59 (20.3) Hospital: 20 (6.9)	NM	Home: 42 (84.0) Nursing home: 4 (8.0) Assisted living facility: 3 (6.0) Unknown: 1 (2.0)
Ambulatory status, *n* (%)							
COVID +	NM	Walk unaided: 12 (14.6) One-stick: 41 (50.0) Two-stick: 25 (30.5) Frame: 4 (4.9) Wheel chair: 0 (0) Bed bound: 0 (0)	NM	NM	NM	NM	Community ambulator without assist: 2 (22.2) Community ambulator with assist: 1 (11.1) Household ambulator with assist: 3 (33.3) Bedbound/wheelchair bound: 2 (22.2) Unknown:1 (11.1)
COVID −	NM	Walk unaided: 38 (11.2) One-stick: 156 (45.9) Two-stick: 104 (30.6) Frame: 35 (10.3) Wheel chair: 0 (0) Bed bound: 0 (0)	NM	NM	NM	NM	Community ambulator without assist: 23 (46.0) Community ambulator with assist: 10 (20.0) Household ambulator with assist: 12 (24.0) Bedbound/wheelchair bound: 4 (8.0) Unknown: 1 (2.0)
ASA grade, *n* (%) or median							
COVID +	I: 2 (1.7) II: 13 (11.1) III: 88 (75.2) IV: 12 (10.3) V: 2 (1.7)	I: 3 (3.7) II: 37 (45.1) III: 36 (43.9) IV: 6 (7.3)	NM	NM	NM	NM	Median-3 (Q1-3, Q3-3)
COVID −		I: 1 (0.3) II: 172 (50.5) III: 158 (46.5) IV: 9 (2.7)	NM	NM	NM	NM	Median-2 (Q1-2, Q3-3)
Anaesthesia, *n* (%)							
COVID +	NM	GA: 16 (19.5) SA: 66 (80.5)	NM	GA:7 (41.2), SA: 6 (35.3)/GA: 8 (57.1), SA: 6 (42.9)* Total GA: 15 (55.5), Total SA: 12 (44.4)	NM	NM	SA: 5 (55.6) GA: 0 (0)
COVID −		GA: 58 (17.1) SA: 282 (82.9)		GA: 67 (62.6) SA: 40 (37.4)			GA: 9 (18.0) SA: 41 (82.0)
Time to surgery							
COVID +	2.4 ± 2.2 (d)	Median: 3 (d)	51.2 (h)	2.7 ± 3.9/2.1 ± 2.1* (d)		52.8 ± 30.1 (h)	29.9 (17.0−49.4) (h)
COVID −		Median: 3 (d)		1.1 ± 0.6 (d)		29.8 ± 26.1 (h)	21.5 (17.1−26.2) (h)
Smoking, *n* (%)							

Table 1 (*continued*)

Study (country)	Vives et al.[16] (Spain)	Kayani et al.[18] (UK)	Thakrar et al.[19](UK)	Egol et al.[20] (USA) (COVID + & COVID suspect* vs. COVID −)	Hall et al.[21] (UK)	Chui et al.[24] (UK)	LeBrun et al.[35] (USA)
Study design	Multicentre, retrospective cohort study	Multicentre retrospective cohort study	Prospective cohort study	Multiple-hospital retrospective study	Multicentre retrospective cohort study	Prospective cohort study	Multicentre retrospective cohort study.
COVID +	NM	Current: 17 (20.7) Previous: 7 (8.5) Nil: 58 (70.7)	NM	Never: 9 (52.9)/6 (42.9)* Former: 6 (35.3)/7 (50.0)* Current: 2 (11.8)/1 (7.1)*	NM	NM	Current smoker: 0 (0) Former smoker: 1 (11.1) Never smoke: 2 (22.2) Unknown: 6 (66.7)
COVID −	NM	Current: 58 (17.1) Previous: 17 (5.0) Nil: 265 (77.9)	NM	Never: 70 (65.4) Former: 27 (25.2) Current: 10 (9.3)	NM	NM	Current smoker: 2 (4.0) Former smoker: 14 (28.0) Never smoke: 32 (64.0) Unknown: 2 (4.0)
Fracture type, *n* (%)							
COVID +	FN: 52 (38.2) IT: 84 (61.8)	FN: 60 (73.2) IT: 12 (14.6) ST: 10 (12.2)	NM	FN: 10 (58.8)/9 (64.3)* IT: 7 (41.2)/5 (35.7)* ST: 0 (0)/0 (0)*	NM	NM	FN: 3 (33.3) IT: 6 (66.7)
COVID −		FN: 272 (80.0) IT: 38 (11.2) ST: 30 (8.8)	NM	FN: 52 (48.6) IT: 48 (44.9) ST: 7 (6.5)	NM	NM	FN: 20 (40.0) IT: 28 (56.0) ST: 2 (4.0)
Surgical techniques, *n* (%)							
COVID +	Surgical treatment: 124 (91.2) Non-operative: 12 (8.8)	CS: 7 (8.5) Hemi A: 42 (51.2) THA: 10 (12.2) DHS: 9 (11.0) IMN: 14 (17.1)	DHS: 7 (16.3) CS: 3 (7.0) Hemi A: 15 (34.9) IMN: 13 (30.2) THA: 1 (2.3) Rev THA: 4 (9.3)	IMN: 5 (38.5)/5 (35.7)* CRPP: 3(23.1)/2 (14.3)* Hemi A: 5 (38.5)/ 7(50.0)* Non-operative: 4 (3.5)*	Fixation: 15 (55.6) Arthroplasty: 10 (37.0) Non-operative: 2 (7.4)	DHS: 3 (25.0) Hemi A: 9 (75.0)	CRPP: 1 (11.1) Hemi A: 2 (22.2) THA: 0 (0) CMN: 4 (44.4) ORIF: 0 (0) Non-operative: 2 (22.2)
COVID −		CS: 46 (13.5) Hemi A: 189 (55.6) THA: 37 (10.9) DHS: 36 (10.6) IMN: 32 (9.4)		IMN: 54 (50.5) Hemi A: 30 (28.0) THA: 6 (5.6) SHS: 7 (6.5) CRPP: 10 (9.3)	Fixation: 157 (54.1) Arthroplasty: 121 (41.7) Non-operative: 12 (4.1)	DHS: 6 (17.1) CS: 3 (8.6) Hemi A: 9 (25.7) IMN: 12 (34.3) THA: 3 (8.6) Revision: 2 (5.7)	CRPP: 4 (8.0) Hemi A: 11 (22.0) THA: 2 (4.0) CMN: 32 (64.0) ORIF: 1 (2.0) Non-operative: 0 (0)

[#] For Newcastle–Ottawa scale, a score of 9 was considered as low risk of bias, 7 or 8 as moderate risk, and 6 or less as high risk of bias.
* Mark indicates the COVID suspect group.
NOS: Newcastle–Ottawa scale; BMI: body mass index; NM: not mentioned; ASA: American Society of Anesthesiologists; SA: spinal anaesthesia; GA: general anaesthesia; NF: femoral neck fracture; IT: intertrochanteric fracture; ST: subtrochanteric fracture; DHS: dynamic hip screw; hemi A: Hemiarthroplasty; CS: cannulated screw; IMN: intramedullary nail; THA: total hip arthroplasty; CRPP: closed reduction percutaneous pinning; CMN: closed medullary nailing; ORIF: open reduction internal fixation; SHS: sliding hip screw.

did not reveal a significant difference (*OR* = 9.24, $p = 0.05$). There was a significant delay in surgery among the COVID-19 + patients compared to COVID-19 − patients with hip fractures (MD = 13.62, 95% *CI*: 5.12–22.12, $p = 0.002$). Three studies[18,20,35] ($n = 619$) reported the details of types of anaesthesia used for surgery. Eighty-three of 122 COVID-19 + patients and 363 of 497 COVID-19 − patients were operated under spinal anaesthesia. The odds of the difference was statistically insignificant (MD = 0.82, 95% *CI*: 0.51–1.30; $p = 0.4$, $I^2 = 18\%$).

Outcome evaluation

Mortality

Each of 4 studies reported 30-day mortality[18–21] and inpatient mortality[16,20,24,35] among the COVID-19 + and COVID-19 − patients with hip fracture (**Table 3**). There was significantly increased risk of death within 30-day (32.2% COVID-19 + death *vs.* 8.9% COVID-19 − death) and during inpatient admission (29.3% COVID-19+ death *vs.* 2.6% COVID-19 − death) among COVID-19 + patients with *OR* of 4.84 (95% *CI*: 3.13–7.47, $p < 0.00001$) and 15.12 (95% *CI*: 6.12–37.37, $p < 0.00001$), respectively (**Fig. 3**).

Critical care admission, length of hospital stay, readmission and discharge to nursing home/rehab (Table 3)

Four studies[18,20,24,35] ($n = 666$) reported critical care admission of the patients with hip fracture during the perioperative period. There was significantly increased need of critical care admission among COVID-19 + patients (*OR* = 5.08, 95% *CI*: 1.49- 17.30, $p < 0.009$, $I^2 = 75\%$, Fig. 3). Two studies ($n = 185$ patients) mentioned about the length of hospital stay.[18,20] The COVID-19 + patients remained admitted for a significantly longer duration of time in hospital (MD = 3.6, 95% *CI*: 1.74–5.45, $p = 0.0001$). Kayani et al.[18] reported the meantime from surgery to hospital discharge, and it was significantly longer among COVOD + patients (13.8 ± 4.6 days) compared to COVID-19 − (6.7 ± 2.5 days) patients. The time from injury to surgery was not different between these 2 groups in that study (median time 3 days). Regarding readmission or ongoing admission within 30-day, there was no difference between COVID-19 + and COVID-19 − patients (MD = 1.38, $p = 0.72$).[18,20,35]

Table 2
Preoperative co-morbidities among COVID-19 + and COVID-19 − patients.

Study (country)	COVID status	Comorbidity index	Smoking status, *n* (%)	Lung diseases, *n* (%)	Cardiovascular disorders (MI/CHF), *n* (%)	Hypertension, *n* (%)	Diabetes mellitus, *n* (%)	Renal failure, *n* (%)	Immunocompromised, *n* (%)	Neurological disorders, *n* (%)
Kayani et al.[18] (UK)	COVID + (*n* = 82)	CFS: 4.6 ± 1.7	Current: 17 (20.7) Previous: 7 (8.5) Nil: 58 (70.7)	45 (54.8)	18 (22.0)	NM	NM	NM	Malignancy: 10 (12.2)	Dementia: 36 (43.9) Neurological: 13 (15.9)
	COVID − (*n* = 340)	CFS: 5.0 ± 1.9	Current: 58 (17.1) Previous smoker: 17 (5.0) Nil: 265 (77.9)	NM	NM	NM	NM	NM	Malignancy: 36 (10.6)	Dementia: 154 (45.6)
Thakrar et al.[19] (UK)	COVID +	NHFS: 5.2	NM	NM	NM	NM	NM	NM	NM	NM
	COVID −	CHS: 4.6	NM	NM	NM	NM	NM	NM	NM	NM
Egol et al.[20] (USA)	COVID + (*n* = 17)	CCI: 2.1 ± 1.8	Never: 9 (52.9) Former: 6 (35.3) Current: 2 (11.8)	4 (23.52)	8 (47.1)	11 (64.7)	7 (41.2)	4 (23.5)	1 (5.9)	6 (35.3)
	COVID suspect (*n* = 14)	CCI: 1.6 ± 1.6	Never: 6 (42.9) Former: 7 (50.0) Current: 1 (7.1)	6 (42.9)	6 (42.9)	11 (78.6)	2 (14.3)	1 (7.1)	1 (7.1)	1 (7.1)
	COVID − (*n* = 107)	CCI: 1.2 ± 1.5	Never: 70 (65.4) Former: 27 (25.2) Current: 10 (9.3)	23 (21.5)	40 (37.4)	67 (62.6)	20 (18.7)	8 (7.8)	4 (3.7)	27 (25.2)
Hall et al.[21] (UK)	COVID + (*n* = 27)	NHS: 5.3 ± 1.7	NM	NM	NM	NM	NM	NM	NM	NM
	COVID − (*n* = 290)	NHS: 4.7 ± 1.7	NM	NM	NM	NM	NM	NM	NM	NM
Chui et al.[24] (UK)	COVID + (*n* = 12)	CFS: 5.7 NHFS: 6.3	NM	NM	NM	NM	NM	NM	NM	NM
	COVID -(*n* = 35)	CFS: 4.2 NHFS: 4.4	NM	NM	NM	NM	NM	NM	NM	NM
LeBrun et al.[35] (USA)	COVID + (*n* = 9)	CCI: 6.0 ± 1.5	Current smoker: 0 (0) Former smoker: 1 (11.1) Never smoke: 2 (22.2) Unknown: 6 (66.7)	1 (11.1)	1 (11.1)	NM	3 (33.3)	1 (11.1)	Malignancy: 2 (22.2)	Dementia: 6 (66.7) History of stroke: 1 (11.1)
	COVID − (*n* = 50)	CCI: 5.7 ± 1.8	Current smoker: 2 (4.0) Former smoker: 14 (28.0) Never smoke: 32 (64.0) Unknown-2 (4.0)	7 (14.0)	12 (24.0)	NM	14 (28.0)	5 (10.0)	Malignancy: 9 (18.0)	Dementia:17 (34.0) History of stroke: 5 (10.0)

CFS: clinical frailty scale; NHFS: Nottingham hip fracture score; CCI: Charlson comorbidity index; NM: not mentioned; MI: myocardial infarction; CHF: congestive heart failure.

Three studies reported the number of patients discharged to nursing home/rehab/hospital. Fifty-five of 122 COVID-19 + patients were discharged to hospital/assisted care centre and 161/497 COVID-19 − patients were discharged to hospital/assisted care centre; this difference was not significant (*OR* = 1.36) (**Fig. 4**).

Complications

Two studies[18,21] (*n* = 560) reported the overall complication rate between COVID-19 + and COVID-19 − patients with hip fracture (**Table 3**). There was a significantly increased risk of major complications among the COVID-19 + group (*OR* = 17.22, 95% *CI*: 9.50−31.19, $p < 0.00001$). The odds of development of pneumonia or respiratory complications was 22.25 times higher among COVID-19 + patients compared to COVID-19 − patients[20,24,35] (**Fig. 4**). Pooled data of 3 studies[20,24,35] (*n* = 244) revealed *OR* of 32.96 for development of acute respiratory distress syndrome/acute respiratory failure among COVID-19 + patients compared to COVID-19 − patients with hip fracture (95% *CI*: 8.08−134.44, $p < 0.00001$).

Publication bias

For the 30-day mortality and inpatient mortality, there was no obvious publication bias as revealed from the symmetry of the funnel plot (**Fig. 5**).

Discussiond

The main findings of this meta-analysis were increased inpatient mortality and 30-day mortality among hip fracture patients who were COVID-19 + compared to COVID-19 −. The odds of the need for critical care admission were 5.08 times higher in COVID-19 + patients. The length of hospital stay, overall complications, risks of acute respiratory failure and pneumonia were higher in hip fracture patients with COVID-19 + status.

Timely surgical intervention for hip fracture is essential to reduce the morbidity and mortality.[36,37] The Norwegian hip fracture registry data showed an increased incidence of 3-day mortality and 1-year mortality when the surgery was delayed over 48 h.[36] It

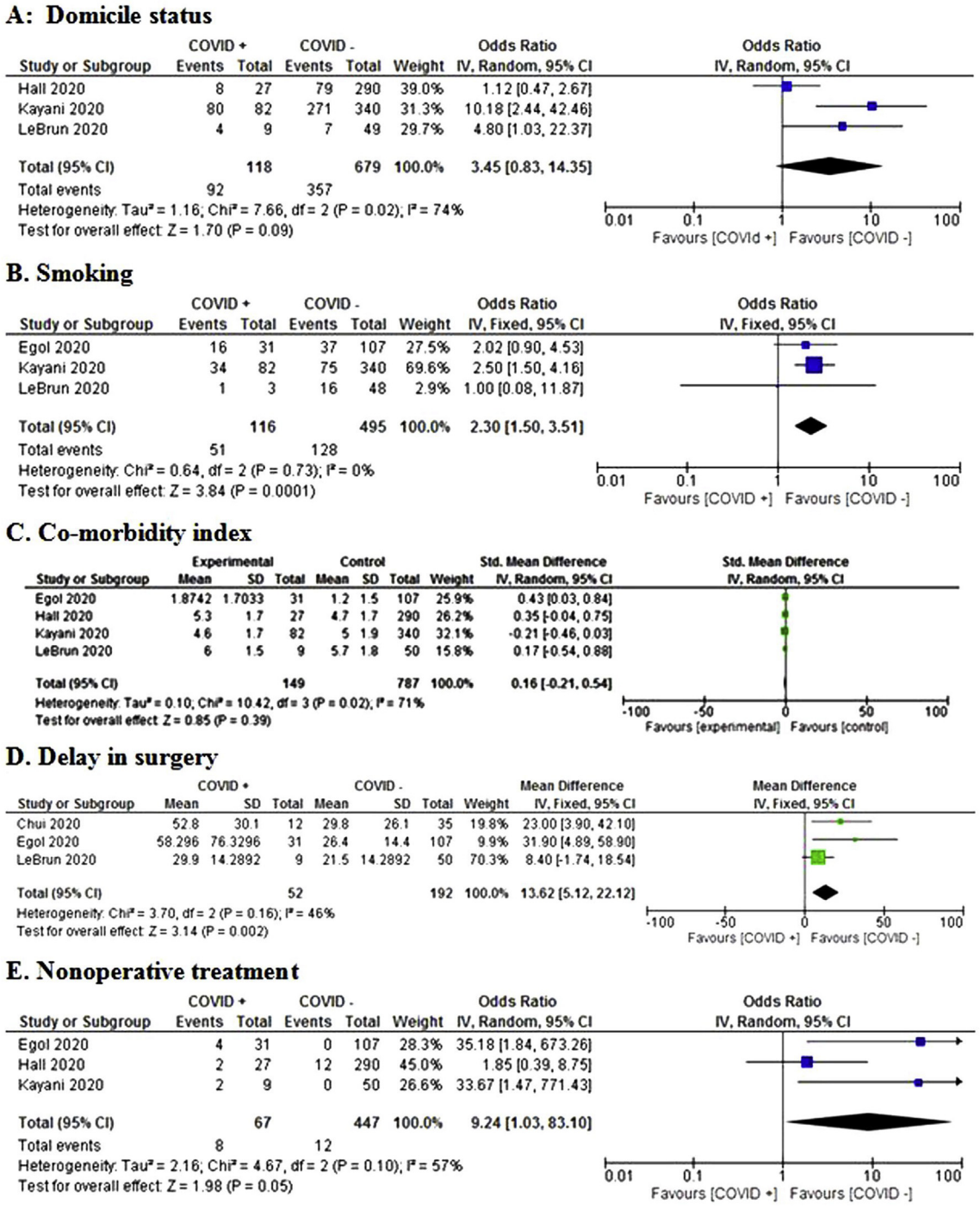

Fig. 2. Forest-plot diagram showing domicile status, smoking, comorbidity index, delay in surgery and nonoperative treatment of hip fracture patients (COVID-19 + *vs.* COVID-19 −).

has been reported that hip fracture surgery performed within 24 h of admission is associated with less pulmonary complications (such as pneumonia) and less need for mechanical ventilation.[37] It is also associated with a shorter hospital stay. At the middle of a severe infectious respiratory disease pandemic, early stabilization of the hip fracture might be crucial to prevent further respiratory compromise. Catellani et al.[23] from Italy reported 16 proximal femur fractures among elderly patients who were COVID-19 + with respiratory symptoms of shortness of breath, desaturation and fever. They observed stabilization of the respiratory parameters once the fracture was surgically fixed. It was possible because they could mobilize the patient after surgery with general patient comfort and improved physiological ventilation. Chui et al.[24] could operate 61% of hip fractured patients within 36 h, and they did not notice a significant difference in mortality rate between COVID-19 + and COVID-19 − patients. Nevertheless, they stressed upon segregation of these fractured patients into "COVID-19 non-infected site" and "COVID-19 infected site". Availability of operation theatre and medical staff are the main concerns during the COVID-19 pandemic along with the risk of cross-infection. The surgery in all hip fracture

Table 3
Outcome of hip fracture surgery among COVID-19 positive and COVID-19 negative patients.

Variables	Vives et al.[16] (Spain)	Kayani et al.[18] (UK)	Thakrar et al.[19] (UK)	Egol et al.[20] (USA)	Hall et al.[21] (UK)	Chui et al.[24] (UK)	LeBrun et al.[35] (USA)
30-day mortality, *n* (%)							
COVID +	NM	25 (30.5)	4 (33.3)	9 (52.9)/2(14.3)*	9 (33.3)	NM	NM
COVID −	NM	35 (10.3)	3 (9.7)	6 (5.6)	24 (8.3)	NM	NM
Inpatient mortality, *n* (%)							
COVID +	7 (30.4)		NM	6 (35.3)/1 (7.1)*	NM	3 (25.0)	5 (55.5)
COVID −	4 (10.3)		NM	1 (0.9)	NM	2 (5.7)	1 (2.0)
Critical care (ICU/HDU) admission, *n* (%)							
COVID +	NM	50 (61.0)	NM	5 (29.4)/3 (21.4)*	NM	0	3 (33.3)
COVID −	NM	62 (18.2)	NM	18 (16.8)	NM	0	1 (0.2)
Discharge to nursing home/hospital/hospice/rehab, *n* (%)							
COVID +	NM	31 (37.8)	NM	9 (52.9)/11 (78.5)*	NM	NM	4 (44.4)
COVID −	NM	62 (18.2)	NM	83 (77.5)	NM		16 (32.0)
Length of hospital stay (days)							
COVID +	NM	13.8 + 4.6	NM	9.8 ± 5.2/7.0 ± 5.9*	NM	12.6 ± 7.7	6
COVID −	NM	6.7 + 2.5	NM	5.0 ± 2.6	NM	8.7 ± 3.8	8
Readmission/on-going admission, *n* (%)							
COVID +	NM	3 (3.7)	NM	2(11.8)/1 (7.1)*	NM	0	NM
COVID −	NM	20 (5.9)	NM	3 (2.8)	NM	0	NM
Overall complications, *n* (%)							
COVID +	NM	73 (89.0)	NM	13 (76.4)/7 (50.0)*	NM	NM	NM
COVID −	NM	119 (35.0)	NM	8 (7.5)	NM	NM	NM
Sepsis or septic shock, *n* (%)							
COVID +	NM	9 (11.0)	NM	3(17.6)/1(7.1)*	NM	NM	NM
COVID −	NM	NA	NM	3 (2.8)	NM	NM	NM
Pneumonia/respiratory infection, *n* (%)							
COVID +	NM	11 (13.4)	NM	12 (70.5)/5 (35.7)*	NM	3 (25.0)	6 (66.6)
COVID −	NM	NA	NM	1 (0.9)	NM	2 (5.7)	5 (10.0)
Deep vein thrombus/pulmonary embolism, *n* (%)							
COVID +	NM	11 (13.4)	NM	2 (11.8)/0 (0)*	NM	NM	NM
COVID −	NM	NA	NM	3 (2.8)	NM	NM	NM
Myocardial infarction/cardiac arrest/cardiac complications, *n* (%)							
COVID +	NM	2 (2.4%)	NM	4(23.6)/0 (0)*	NM	NM	NM
COVID −	NM	NA	NM	3 (2.8)	NM	NM	NM
Acute renal failure/acute kidney injury, *n* (%)							
COVID +	NM	10 (12.2)	NM	3 (17.6)/1 (7.1)*	NM	NM	NM
COVID −	NM	NA	NM	8 (7.5)	NM	NM	NM
Stroke							
COVID +	NM		NM	0 (0)/0 (0)*	NM	NM	NM
COVID −	NM		NM	2 (1.9)	NM	NM	NM
Acute respiratory failure/ARDS, *n* (%)							
COVID +	NM	8 (9.8)	NM	7 (41.2)/4 (28.6)*	NM	0	3 (33.3)
COVID −	NM	NA	NM	2 (1.9)	NM	0	0

*: COVID-19 suspect.
NM: not mentioned; NA: not available; ARDS: acute respiratory distress syndrome.

patients got delayed in the studies of this review.[16–20,24,35] However, this delay was significantly longer among the COVID-19 + patients compared to COVID-19 − patients (MD = 13.62 h). Probably, the medical optimization of COVID-19 + patients for surgery took a longer time.

Cheung et al.[17] from the USA reported that there was an increased need for supplemental oxygen for a temporary period in the postoperative period among asymptomatic or mild COVID-19 symptomatic patients ($n = 10$) with hip fracture. They advocated that such asymptomatic or mild variant COVID-19 symptomatic patients can safely undergo early surgical fixation after appropriate medical optimization. In agreement with the study,[17] this review noted an increased need of critical care admission (ICU/HDU) among COVID-19 + patients irrespective of their symptoms in the preoperative period.

Segarra et al.[27] from Spain compared the mortality of orthopaedic trauma patients who were operated on during COVID-19 pandemic to a similar cohort of patients operated in the year 2019. They did not find a significant difference in 30-day mortality between these 2 cohorts. The predominant fracture in their series was hip fracture (52.8%). They advocated that with proper screening protocol, hip fracture surgery and even elective procedure can be safely performed during this pandemic. Similar results were published by Malik-Tebassum et al.,[38] who did not notice a difference in mortality, complications and time to surgery among the hip fracture patients during the pandemic period compared to pre-pandemic time. However, studies reporting the comparison of COVID-19 + and COVID-19 − patients with associated hip fracture had a different result.[16,18–21,24,35] These researchers noted increased early mortality, increased length of hospital stay, a higher incidence of major complications, and a greater incidence of ventilator need in COVID-19 + patients compared to COVID-19 − patients. Vives et al.[16] reported higher mortality even within a follow-up period of 14 days compared to the 30-day mortality rate of the Spanish Registro Nacional de Fracturas de Cadera[39] and other national registries of Europe.[40] The odds of death within 30-day period were 4.84 times higher in the COVID-19 + patients as per this meta-analysis. The inpatient death rate was even higher ($OR = 15.12$).

Presence of multiple comorbidities (≥3 comorbidities) was associated with an increased risk of mortality among COVID-19 + patients.[18,41] The report of COVID-19-Surg Collaborative group on 30-day mortality in 1128 patients from 24 countries who underwent emergency and elective surgery during the early period of COVID-19 pandemic was appalling.[26] The overall 30-day mortality was 21.1% in the COVID-19 + group, and the majority of these COVID-19 + patients ended up with pulmonary complications

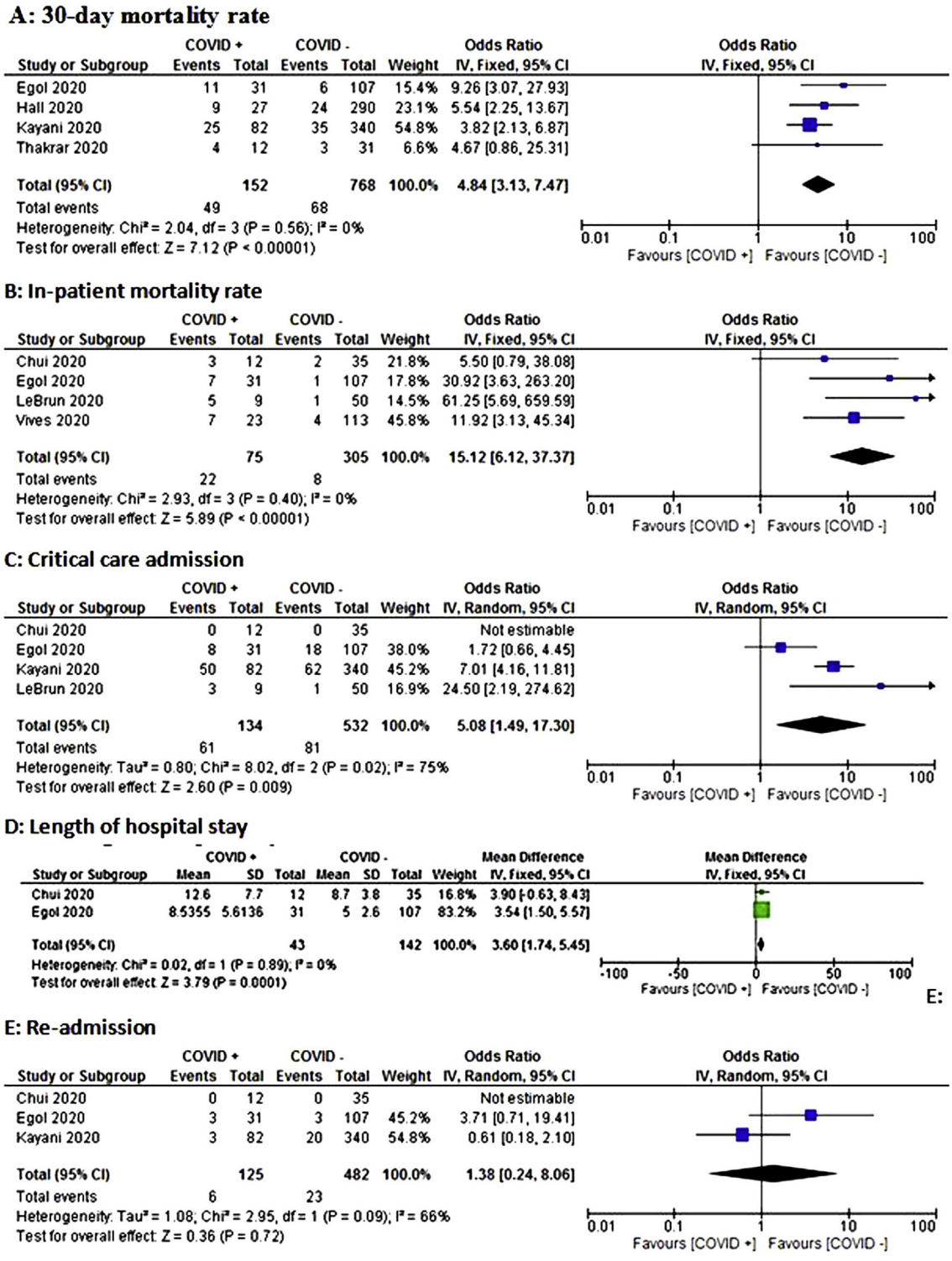

Fig. 3. Forest-plot diagram showing 30-day mortality, inpatient mortality, critical care admission, length of hospital stay and readmission in COVID-19 positive and COVID-19 negative patients.

(48.3%). Deng et al.[42] reported that pre-existing comorbidities increased the risk of mortality from 41.5% to 72.5% among the COVID-19 + patients. Among the pre-existing comorbidities, diabetes mellitus, hypertension and cardiorespiratory diseases were associated with increased risk of complications.[43] We compared the comorbidity indices in both groups. The Charlson comorbidity index, clinical frailty scale and Nottingham hip fracture scores are validated measures of comorbidity and functional status in hip fracture patients.[24] These scores predict 30-day mortality and inpatient mortality in these patients. However, no significant differences in the comorbidity indices were observed between COVID-19 + and COVID-19 − patients. This indicated that COVID-19

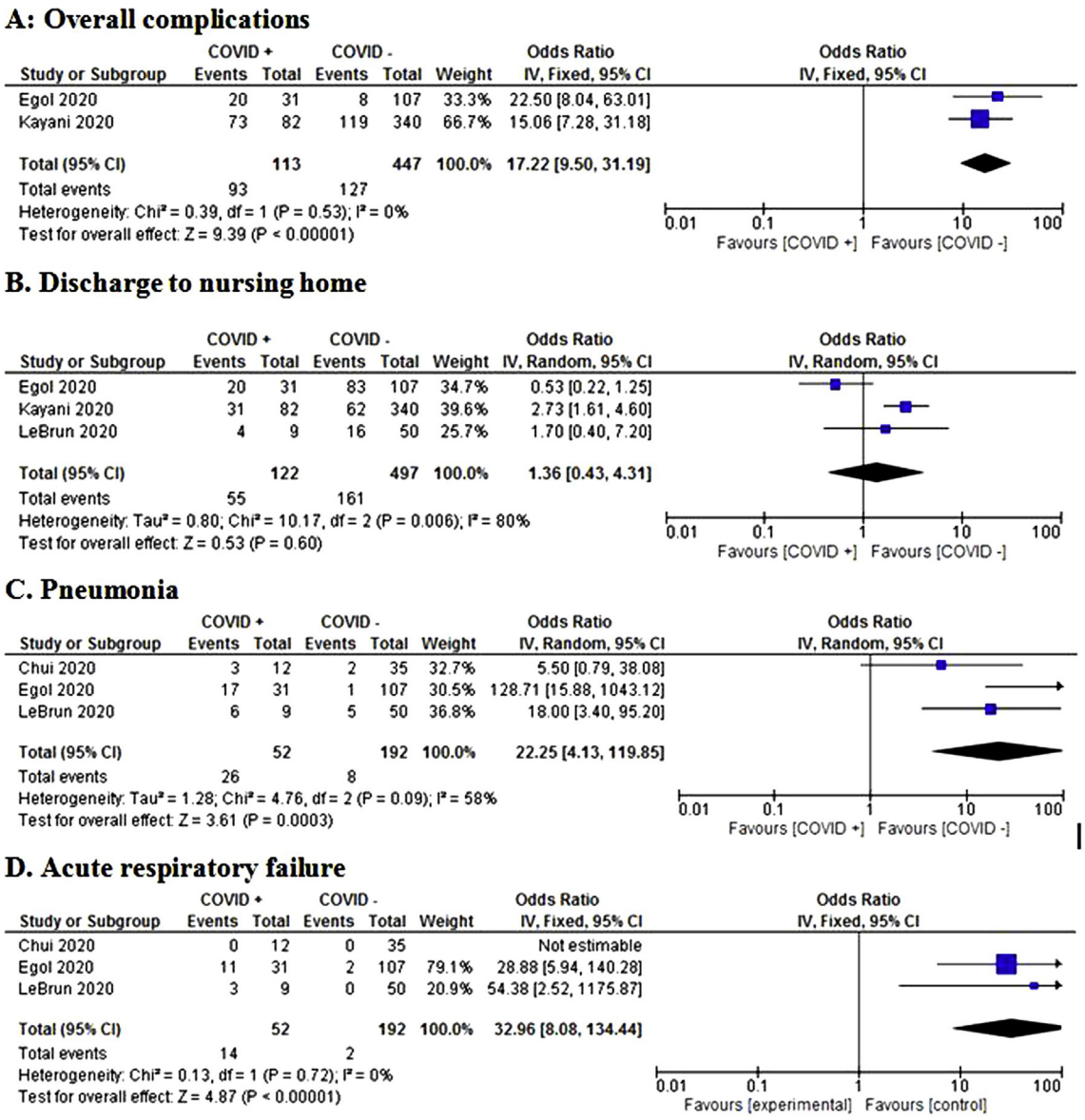

Fig. 4. Forest-plot diagram showing overall complications, discharge to hospital/rehab centre, pneumonia and acute respiratory failure in COVID-19 positive and COVID-19 negative patients.

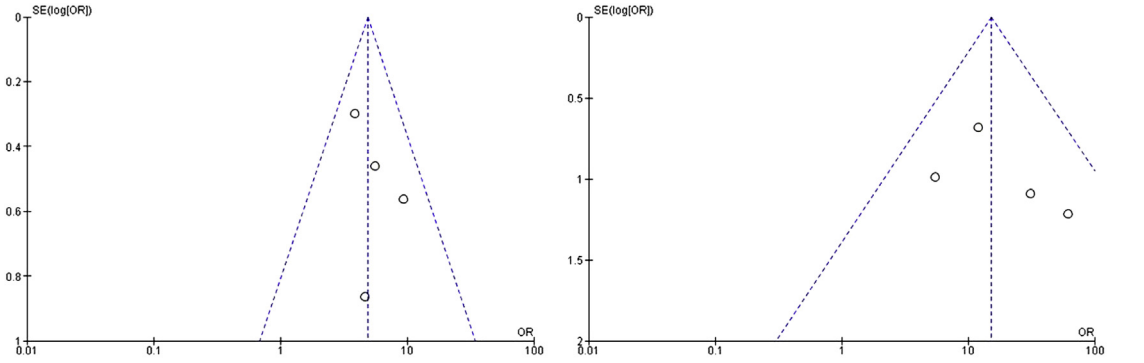

Fig. 5. Funnel plot (symmetrical) for 30-day mortality and inpatient mortality.

infection itself was an independent predictor of mortality in hip fracture patients. A significantly higher incidence of overall major complications, pneumonia and acute respiratory failure was observed in the COVID-19 + patients in the postoperative period. The study by Zhou et al.[44] reported 89% systemic complication among COVID-19 + surgical patients, including respiratory failure (54%), acute respiratory distress syndrome (31%), cardiac problems (23%) and acute kidney injury (15%). They hypothesized that surgical intervention augments the proinflammatory response, which has already been developed in a trauma victim because of the injury (second-hit phenomenon).

Few more observations in this meta-analysis warn the orthopaedic surgeons to be more vigilant in selective groups of patients. Elderly patients with compromised immunity and multiple comorbidities are at an increased risk of COVID-19 infection. These patients live in a closed social set up, mainly in nursing home and rehabilitation centre, which increases their risks of infection.[24] The odds of COVID-19 infectivity among patients staying in closed groups were 3.45 times higher than non-COVID-19 patients (although non-significant). Similarly, active smokers or former smokers had an increased risk ($OR = 2.30$) of COVID-19 infection compared to non-smokers. This review failed to find a difference in types of anaesthesia among COVID-19 + and COVID-19 − patients despite recommendations for the use of regional anaesthesia in COVID-19 + patients. The incidence of readmission was also similar in both groups of patients.

This meta-analysis has certain limitations. Although these studies are from developed nations, the protocol of care may differ among institutes as there is no definite treatment guideline for COVID-19 at this moment. The follow-up time is short; 3 studies have not evaluated even for 30-days. The retrospective study design and small patient cohort are also the main limitations of this meta-analysis. Despite that, this meta-analysis is the first of its kind to report the mortality and morbidity among hip fracture patients during COVID-19 pandemic.

To conclude, there are increased risks of inpatient mortality, 30-day mortality and critical care unit admission among hip fracture patients who have concomitant COVID-19 infection. These patients have significantly increased risks of developing pneumonia and acute respiratory failure in the perioperative period. Despite equivalent comorbidity indices, COVID-19 + patients are prone to death in the perioperative period. With the development of drugs and better treatment protocols of COVID-19, the interpretation of this meta-analysis might change.

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Nil.

Ethical statement

This systematic review/meta-analysis has been registered in PROSPERO. The registration number is: CRD42020200592.

Declaration of competing interest

All the authors states that there is no conflict of interest.

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