Systematic Review

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The impact of COVID-19 on mortality in trauma patients undergoing orthopedic surgery: a systematic review and meta-analysis

Abbreviated title: Orthopedic trauma surgery

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ABSTRACT

Objective: The global spread of the COVID-19 pandemic has affected all aspects, including orthopedic trauma surgery. This study aims to investigate whether COVID-19–positive patients who underwent orthopedic surgery trauma had a higher risk of postoperative mortality.

Methods: ScienceDirect, the Cochrane COVID-19 Study Register, and MEDLINE were searched for original publications. This study adhered to the PPRISMA 2020 statement. The validity was evaluated using a checklist developed by the Joanna Briggs Institute. Study and participant characteristics, as well as the odds ratio, were extracted from selected publications. Data were analyzed using RevMan ver. 5.4.1.

Results: After applying the inclusion and exclusion criteria, 16 articles among 717 total were deemed eligible for analysis. Lower-extremity injuries were the most common condition, and pelvic surgery was the most frequently performed intervention. There were 456 COVID-19–positive patients (6.12%) and 134 deaths among COVID-19–positive patients, revealing a mortality escalation (29.38% vs. 5.30% among COVID-19–negative patients; odds ratio, 7.72; 95% confidence interval, 6.01–9.93; P<0.00001).

Conclusion: Among COVID-19–positive patients, the postoperative death rate increased by 7.72 times. It may be possible to improve prognostic stratification and perioperative care by identifying risk factors.

Keywords: Wounds and injuries; Orthopedic procedures; COVID-19; Mortality

CAPSULE SUMMARY

What is already known

During the COVID-19 pandemic, there was a decrease in emergency room visits for trauma and surgical intervention, particularly in traumatology services.

What is new in the current study

This study analyzes the most recent literature on postoperative mortality in trauma patients undergoing orthopedic surgery during the COVID-19 pandemic.

INTRODUCTION

The World Health Organization (WHO) announced the discovery of a new condition, COVID-19, in early February 2020, before declaring a global pandemic in March 2020. The rapid global spread of the causative pathogen, SARS-CoV-2, has caused major changes to human life worldwide. Many countries in the Asia-Pacific region, including Australia, Korea, and Japan, were among the first to respond to the COVID-19 epidemic [1].

During the COVID-19 pandemic, emergency room visits decreased, particularly visits for trauma and surgical intervention in traumatology cases [2,3]. With this reduction in visits, patients more frequently received delayed care during the current pandemic [4]. Previous studies have shown that delaying surgery increases mortality and the risk of postoperative pneumonia in trauma patients [5].

The present study sought to conduct a systematic review and meta-analysis on postoperative mortality in COVID-19–positive and –negative patients undergoing orthopedic trauma surgery. The present meta-analysis sought to investigate the odds ratio (OR) of mortality in this patient population by comparing statistics between COVID-19–positive and –negative groups. We speculated that postoperative COVID-19–positive orthopedic trauma patients would have a higher risk of death than those negative for COVID-19.

METHODS

Search strategy and study selection

The protocol of this review was registered in PROSPERO (International Prospective Register of Systematic Reviews) on September 27, 2022 (No. CRD42022359112). In accordance with recent PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) 2020 statement for identifying research through databases and registers, a systematic review of the mortality in orthopedic surgery owing to trauma during the COVID-19 pandemic was performed, as shown in Fig. 1 [6]. The phrases "orthopedic" AND "trauma" AND "surgery" AND "COVID-19" were used to search the ScienceDirect and MEDLINE (via PubMed) databases for English-language studies that reported mortality among both COVID-19–positive and –negative patients. The literature search was conducted on September 20, 2022. A search using MeSH (Medical Subject Headings) terms was carried out whenever possible using the combination of the search 1 ("orthopedic trauma surgery" [MeSH Terms] OR "orthopedic trauma surgery" [All Fields]) AND search 2 ("COVID-19 [MeSH Terms] OR "COVID-19" [All Fields]) strategies.

Inclusion and exclusion criteria

We included observational studies like cohort, cross-sectional, and case–control studies but excluded review articles. The validity of the papers included in this study was evaluated using a series of inquiries based on a checklist in line with the kind of study created by the Joanna Briggs Institute [7,8], as shown in Supplementary Table 1 [9–23] and Supplementary Table 2 [24]. Articles that did not fit the requirements for inclusion were rejected. The inclusion criteria formulated according to the PICO mnemonic for clinical research questions were as follows: (1) P (patient, population, problem): patients of all ages who underwent orthopedic trauma surgery; (2) I (intervention, prognostic factor, or exposure): COVID-19 infection (positive or negative polymerase chain reaction result); (3) C (comparison or intervention): none; and (4) O (outcome): postoperative mortality.

Data synthesis

If possible, the data synthesis included information on patient mean age, sex, death rate, underlying disease, complications, intervention site, type of surgery, and hospital stay. The data were summarized in Microsoft Excel (Microsoft Corp) after their collection, and RevMan ver. 5.4.1 (Cochrane Collaboration) was used for statistical analysis. We performed planned subgroup analyses for the confounding variables, which included time points of patient outcome measurement (inpatient vs. 30-day follow-up) and age (<60 years vs. >60 years). Publication bias was measured by visual inspection of funnel plots and quantitatively using Egger test [25]. We considered findings significant if $P<0.05$. GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) scores were used to evaluate the certainty of the evidence for each outcome [26]. A GRADE summary of the findings in Table 3 was generated using GRADEpro (GradePro Inc) [27].

RESULTS

During the literature search, 717 studies were discovered. After removing duplicates, 691 studies remained, and 32 potentially relevant studies were chosen for eligibility examination. This meta-analysis included 16 observational studies (10 retrospective cohort studies, five prospective cohort studies, and one cross-sectional study). The majority of patients in these investigations were >60 years old. The study characteristics and postoperative mortality findings are shown in Table 1 [9–24]. The most common injury sites were the hip and femur, followed by other lower-limb sites such as the patella, tibia, ankle, foot, and upper limb. Supplementary Table 3 shows the types of injuries that required orthopedic surgery. Hemiarthroplasty, total hip arthroplasty, unspecified elective minor surgery, and open reduction and internal fixation of the femur were the major surgeries performed.

Five studies [15,18,20,21,24] compared the number of orthopedic surgeries performed during and before the start of the COVID-19 pandemic and discovered that the numbers of surgeries performed did not significantly differ. Nonetheless, postoperative mortality increased significantly during the pandemic.

During the COVID-19 pandemic, 7,795 injuries were reported (Supplementary Table 3), with 15 cases (0.19%) not being treated surgically. According to Table 1 [9–24], we identified 6,996 COVID-19–negative patients (93.89%) and 456 COVID-19–positive patients (6.11%) among the 7,452 operative patients who underwent COVID-19 testing via polymerase chain reaction testing of a nasopharyngeal swab. Meanwhile, 134 COVID-19–positive patients (29.38%) died after surgery compared to 5.30% of the COVID-19–negative group, despite the small number of COVID-19–positive patients. The mortality rate of COVID-19–positive patients ranged from 14.28% to 50% among included studies.

Complications due to COVID-19 were most commonly reported as the primary cause of postoperative death among COVID-19–positive patients. The reported primary causes of postoperative death, complications, underlying disease, and mean hospital stay in both groups are shown in Table 2 [9–24]. Eight studies [11–15,19,20,22] did not report the cause of death in their research.

A total of 1,616 reported surgeries from seven studies [13,16–18,20–22] are shown in Supplementary Table 4. In contrast, nine studies [9–12,14,15,19,23,24] did not specify the surgeries performed in their studies. Only Lim et al. [18] reported the type of anesthesia used in both groups.

Fig. 2 depicts the qualitative analysis of each study's funnel plot to determine the degree of asymmetry. Egger regression test was calculated with P=0.34. A funnel plot and Egger test showed no evidence of publication bias. As shown in Figs. 3–6 [9–24], we established a forest plot and subgroup analysis to illustrate the significance among all studies included in our meta-analysis. We analyzed the 16 trials and established a random-effects model, resulting in an overall OR of 7.72 (95% confidence interval [CI], 6.01–9.93; P<0.00001; I^2=0%). As shown in Fig. 6 [13–15,17,23], the incidence of venous thromboembolism (VTE) was increased among COVID-19–positive patients (OR, 4.08; 95% CI, 1.23–13.58). According to these findings, COVID-19 positivity might increase the mortality rate and occurrence of thromboembolism in patients undergoing orthopedic surgery.

The test for subgroup differences in Figs. 4 and 5 [9–24] indicated a statistically significant subgroup effect (P<0.05) at inpatient (OR, 8.67; 95% CI, 5.82–12.91), 30-day follow-up (OR, 7.32; 95% CI, 4.30–12.49), and in patients with a mean age of >60 years (OR, 7.75; 95% CI, 6.02–9.97). Mortality in COVID-19–positive patients with a mean age of <60 years showed an increase in one study, but this increase was not statistically significant (OR, 5.75; 95% CI, 0.46–72.30; P = 0.18).

DISCUSSION

This systematic review and meta-analysis looked at the death rate among COVID-19–positive and –negative trauma patients undergoing orthopedic surgery. Most of the participants in this study were >60 years old. This finding is consistent with those of Atinga et al. [28], who found that geriatric trauma cases are increasing every year and now account for >25% of all significant trauma cases in the United Kingdom. Aging is associated with progressive physiological changes that affect various systems. Elderly people respond to trauma in a physiologically different manner than other people. Physiological responses in the elderly might vary due to co-occurring diseases, premorbid frailty, and prescribed drugs.

Previous research has linked hip fracture in the elderly to greater morbidity, a loss of autonomy in activities of daily living, a high rate of institutionalization, and mortality. Conservatively, mortality after hip fracture surgery is high in the first year, being approximately 30% of all cases [29–31]. In this study, 70 of the 134 patients with postoperative deaths among 456 COVID-19–positive patients who underwent orthopedic surgery had a hip or femur fracture.

According to Supplementary Table 4, the most commonly performed procedure in this study was hip arthroplasty. Haskel et al. [32] discovered that hip fracture volume in the elderly did not decrease during the lockdown period, even in areas severely affected by COVID-19 outbreaks. Age, a large waist circumference, a lower skeletal muscle index, bone mass density, vitamin D level, physical function, nutritional status, and cognitive function are linked to hip fractures in the elderly [33,34].

VTE involves both pulmonary embolism and deep vein thrombosis, respectively, and occurs in 0.6% to 1.5% of patients undergoing total joint arthroplasty. The risk factors for VTE are described by Virchow triad, which are venous stasis, endothelial damage, and a hypercoagulable state. VTE is typically the result of the interaction of two or less causes. Venous stasis can occur both during and after surgery due to intraoperative immobilization. Prolonged immobility raises the possibility of VTE development [35].

Previous research found that COVID-19–positive patients had a higher mortality rate during hip and femur fracture surgery [36–39]. Surgery within 48 hours does not correlate with a lower mortality rate in COVID-19–positive patients [13]. As shown in Table 2 [9–24], the mean hospital stay length among COVID-19–positive patients undergoing hip and femur surgery was longer than that among COVID-19–negative patients. This result is in line with the study by Kayani et al. [37], which stated that hip surgery in COVID-19–positive patients was associated with a longer hospital stay, longer immobilization, more hospitalizations in the intensive care unit, an increased chance of peri-operative complications, and greater mortality rates. COVID-19–positive patients with a smoking history and multiple (>3) significant comorbidities have a higher risk of death. Identifying factors that contribute to a higher death rate may improve prognostic classification and interdisciplinary perioperative care.

This review has some limitations. The majority GRADE rating in Table 3 was low because the evidence came from observational studies. Inaccurate studies with smaller sample sizes of COVID-19–positive patients may be influenced by chance. Of the 16 studies, only nine provided information about the type of surgery performed, eight reported the primary cause of postoperative death, and just one provided information about the type of anesthesia used in both groups. All of the included studies were conducted prior to the availability of COVID-19 vaccines.

In conclusion, the postoperative mortality rate among COVID-19–positive patients was 7.72 times greater than that of COVID-19–negative patients. Identifying risk factors for increased mortality may improve prognostic classification and perioperative interdisciplinary medication. The findings of this study should be considered by the larger orthopedic community when developing guidelines for treating orthopedic trauma in specific populations in the COVID-19 era.

SUPPLEMENTARY MATERIALS

Supplementary Table 1. Joanna Briggs Institute risk of bias quality assessment for cohort studies

Supplementary Table 2. Joanna Briggs Institute risk of bias quality assessment for cross-sectional studies

Supplementary Table 3. Indications for orthopedic surgery during the COVID-19 pandemic

Supplementary Table 4. The reported surgery in this study

Supplementary Material 1. PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) checklist.

Supplementary materials are available at https://doi.org/10.15441/ceem.22.403.

ETHICS STATEMENTS

Not applicable.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Conceptualization: HDP; Formal analysis: VH, RP; Methodology: all authors; Project administration: HDP; Writing–original draft: HDP; Writing–review & editing: all authors. All authors read and approved the final manuscript.

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FIGURE LEGENDS

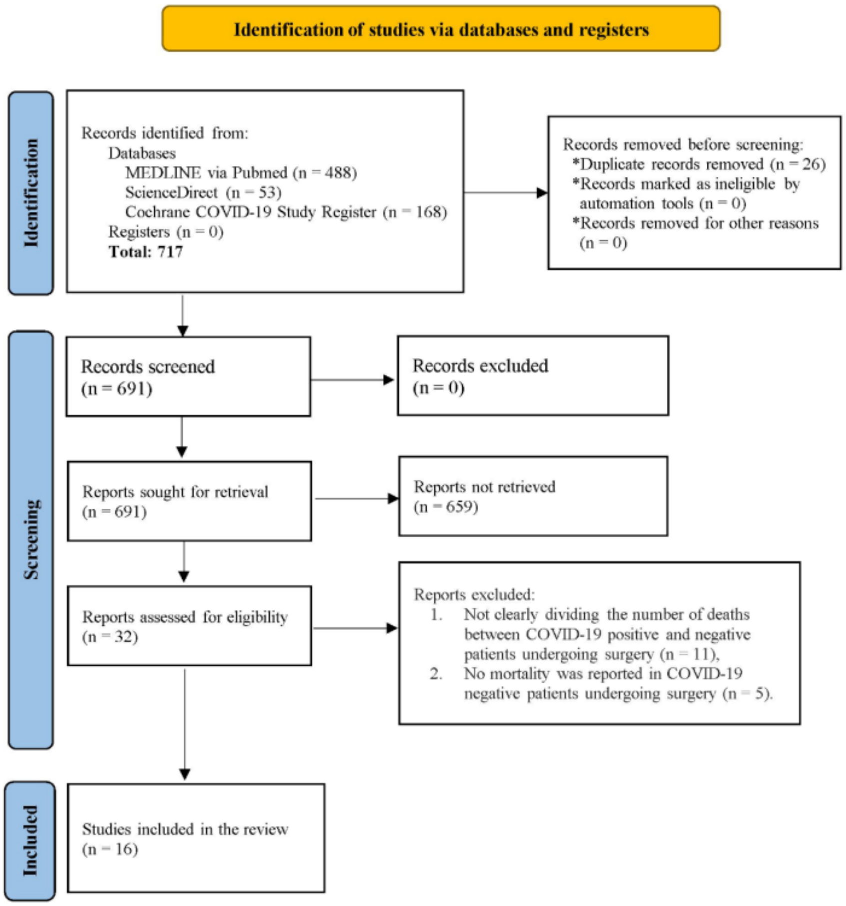


Fig. 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 statement flowchart of the search strategy and selection of studies.

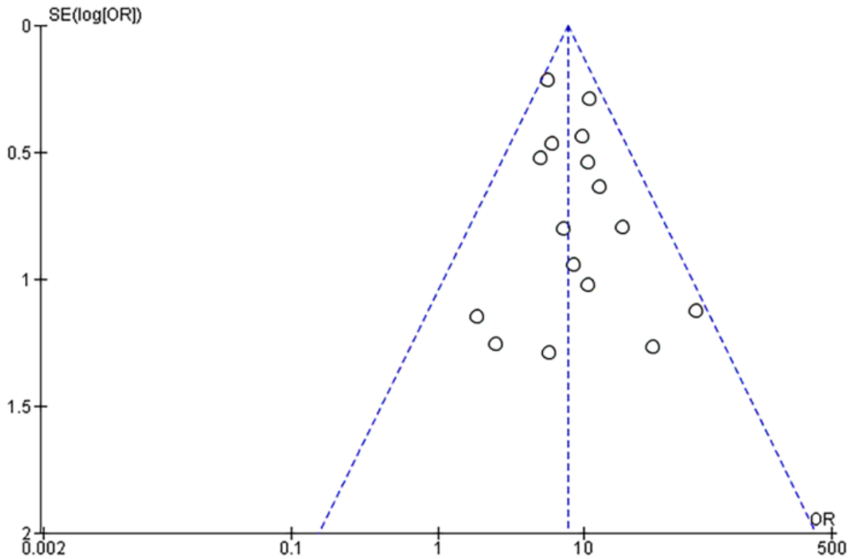


Fig. 2. No publication bias is visible in the funnel plot of the selected studies. This figure displays the qualitatively evaluated asymmetry findings from each study. SE, standard error; OR, odds ratio.

Study or Subgroup	COVID-19 + Events	COVID-19 + Total	COVID-19 - Events	COVID-19 - Total	Weight	Odds Ratio M-H, Random, 95% CI
Andrzejowski et al	4	12	4	150	2.6%	18.25 [3.84, 86.67]
Balakumar et al	19	43	11	146	8.5%	9.72 [4.11, 22.96]
Beaven et al	9	40	8	145	5.9%	4.97 [1.78, 13.91]
Clement et al	22	68	63	1501	19.6%	10.92 [6.19, 19.25]
Dallari et al	8	53	7	424	5.6%	10.59 [3.67, 30.57]
Egol et al	6	17	1	107	1.3%	57.82 [6.37, 525.04]
Fisher et al	2	10	1	24	1.0%	5.75 [0.46, 72.30]
Greensmith et al	2	5	5	84	1.6%	10.53 [1.42, 78.18]
Hall et al	9	25	24	278	7.5%	5.95 [2.38, 14.90]
LeBrun et al	3	7	1	40	1.0%	29.25 [2.43, 351.43]
Lim et al	1	7	7	85	1.2%	1.86 [0.19, 17.69]
Pass et al	32	123	214	3610	34.7%	5.58 [3.65, 8.54]
Sobti et al	3	6	5	47	1.8%	8.40 [1.32, 53.40]
Thakrar et al	4	12	1	6	1.0%	2.50 [0.21, 29.25]
Wright et al	5	16	3	50	2.5%	7.12 [1.47, 34.39]
Zajonz et al	5	12	16	299	4.0%	12.63 [3.61, 44.24]
Total (95% CI)		**456**		**6996**	**100.0%**	**7.72 [6.01, 9.93]**
Total events	134		371			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 13.87$, $df = 15$ ($P = 0.54$); $I^2 = 0\%$
Test for overall effect: $Z = 15.96$ ($P < 0.00001$)

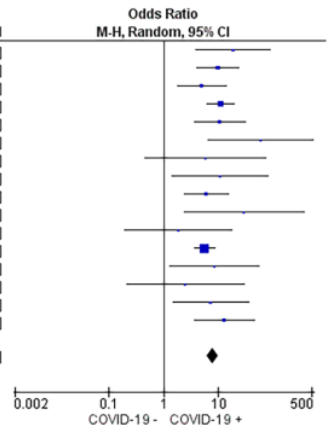


Fig. 3. Forest plot of all the articles included in this study. M-H, Mantel-Haenszel test; Random, random-effects model; CI, confidence interval.

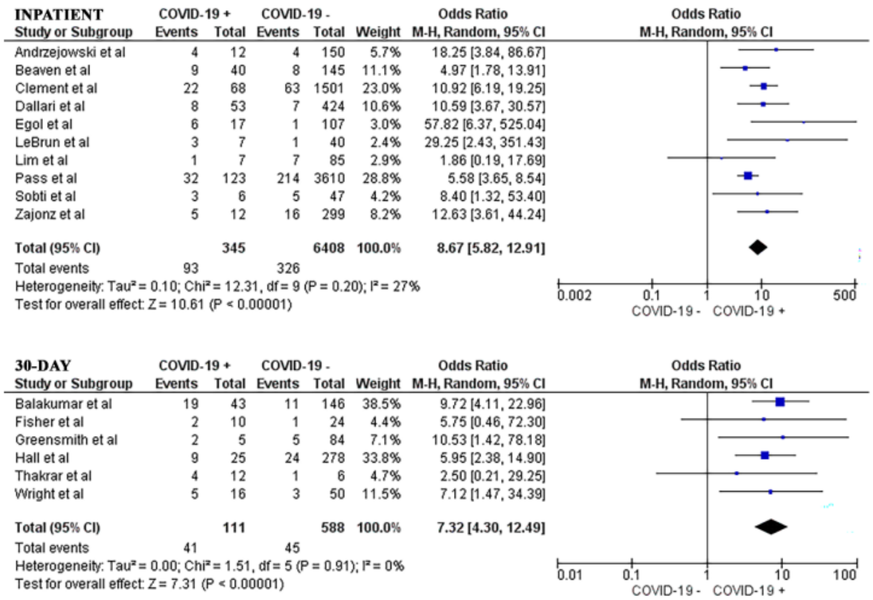
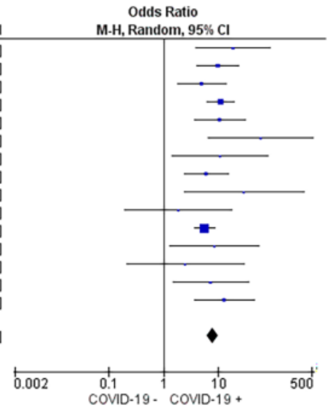


Fig. 4. Postoperative mortality of (A) At inpatient and (B) 30-day follow-up. M-H, Mantel-Haenszel test; Random, random-effects model; CI, confidence interval.

>60 YEARS	COVID-19 +		COVID-19 -			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Andrzejowski et al	4	12	4	150	2.6%	18.25 [3.84, 86.67]
Balakumar et al	19	43	11	146	8.6%	9.72 [4.11, 22.96]
Beaven et al	9	40	8	145	6.0%	4.97 [1.78, 13.91]
Clement et al	22	68	63	1501	19.8%	10.92 [6.19, 19.25]
Dallari et al	8	53	7	424	5.7%	10.59 [3.67, 30.57]
Egol et al	6	17	1	107	1.3%	57.82 [6.37, 525.04]
Greensmith et al	2	5	5	84	1.6%	10.53 [1.42, 78.18]
Hall et al	9	25	24	278	7.6%	5.95 [2.38, 14.90]
LeBrun et al	3	7	1	40	1.0%	29.25 [2.43, 351.43]
Lim et al	1	7	7	85	1.3%	1.86 [0.19, 17.69]
Pass et al	32	123	214	3610	35.1%	5.58 [3.65, 8.54]
Sobti et al	3	6	5	47	1.9%	8.40 [1.32, 53.40]
Thakrar et al	4	12	1	6	1.1%	2.50 [0.21, 29.25]
Wright et al	5	16	3	50	2.6%	7.12 [1.47, 34.39]
Zajonz et al	5	12	16	299	4.1%	12.63 [3.61, 44.24]
Total (95% CI)		**446**		**6972**	**100.0%**	**7.75 [6.02, 9.97]**
Total events	132		370			

Heterogeneity: Tau² = 0.00; Chi² = 13.82, df = 14 (P = 0.46); I² = 0%
Test for overall effect: Z = 15.91 (P < 0.00001)



<60 YEARS	COVID-19 +		COVID-19 -			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Fisher et al	2	10	1	24	100.0%	5.75 [0.46, 72.30]
Total (95% CI)		**10**		**24**	**100.0%**	**5.75 [0.46, 72.30]**
Total events	2		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.35 (P = 0.18)

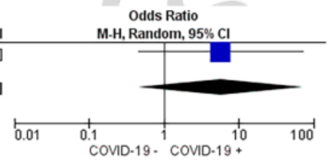


Fig. 5. Postoperative mortality in the patients with a mean age of (A) >60 years and (B) <60 years. M-H, Mantel-Haenszel test; Random, random-effects model; CI, confidence interval.

VTE	COVID-19 +		COVID-19 -			Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Dallari et al	0	53	2	424	15.5%	1.58 [0.07, 33.34]
Egol et al	2	17	3	107	41.3%	4.62 [0.71, 29.97]
Fisher et al	2	10	0	24	14.7%	14.41 [0.63, 331.31]
LeBrun et al	0	7	1	40	13.3%	1.76 [0.07, 47.33]
Zajonz et al	0	12	2	299	15.1%	4.76 [0.22, 104.47]
Total (95% CI)		**99**		**894**	**100.0%**	**4.08 [1.23, 13.58]**
Total events	4		8			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.28$, df = 4 (P = 0.86); $I^2 = 0\%$
Test for overall effect: Z = 2.29 (P = 0.02)

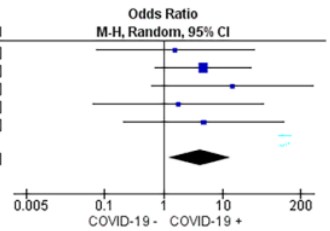


Fig. 6. Occurrence of venous thromboembolism in COVID-19–positive and –negative groups. M-H, Mantel-Haenszel test; Random, random-effects model; CI, confidence interval.

Table 1. Study characteristics and postoperative mortality

Study	Study period	Study design	Study location	Age (yr)	Female sex	Intervention location	Covid-19 (+)		Covid-19 (–)		Follow-up
							Mortality (n=134, 29.38%)	Total surgery (n=456)	Mortality (n=371, 5.30%)	Total surgery (n=6,996)	
Andrzejowski et al. [9]	March 23, 2020–April 22, 2020 (1 mo)	Prospective	UK	60.7 (1–98)	88	Upper limb, hip, lower limb, and other trauma	4 (33.33)	12	4 (2.66)	150	Inpatient
Balakumar et al. [11]	March 26, 2020–May 20, 2020 (56 day)	Prospective	UK	65.0	Not reported	Clavicula, upper limb, hip, lower limb, and other trauma	19 (44.18)	43	11 (7.53)	146	30-day
Beaven et al. [10]	March 28, 2020–May 25, 2020 (59 day)	Prospective	UK	83.0 (76–90)	Not reported	Proximal femur	9 (22.50)	40	8 (5.51)	145	Inpatient
Clement et al. [12]	March 1, 2020–April 19, 2020 (50 day)	Retrospective	Edinburg, UK	60.0 (14–102)	850	Upper limb, hip, lower limb, and other trauma	22 (32.35)	68	63 (4.19)	1,501	Inpatient
Dallari et al. [13]	March 8, 2020–May 4, 2020 (58 day)	Retrospective	Italy	83.3	381	Hip	8 (15.09)	53	7 (1.65)	424	Inpatient
Egol et al. [14]	February 1, 2020–April 15, 2020 (75 day)	Prospective	New York, USA	83.0	78	Hip	6 (35.29)	17	1 (0.93)	107	Inpatient
Fisher et al. [15]	March 16, 2020–May 15, 2020 (61 day)	Retrospective	New York, USA	58.0	10	Not reported	2 (20.0)	10	1 (4.16)	24	30-day
Greensmith et al. [24]	March 14, 2020–May 28, 2020 (76 day)	Cross-sectional	UK	81.6 (51–103)	Not reported	Hip	2 (40.0)	5	5 (5.95)	84	30-day
Hall et al. [16]	March 1, 2020–April 15, 2020 (46 day)	Retrospective	UK	80.0 (50–101)	Not reported	Hip	9 (36.0)	25	24 (8.63)	278	30-day
LeBrun et al. [17]	March 20, 2020–April 24, 2020 (36 day)	Retrospective	New York, USA	85.0 (65–100)	Not reported	Hip	3 (42.85)	7	1 (2.50)	40	Inpatient
Lim et al. [18]	March 1, 2020–May 15, 2020 (76 day)	Retrospective	UK	84.9	70	Neck of femur	1 (14.28)	7	7 (8.23)	85	Inpatient
Pass et al. [19]	July 1, 2020–December 31, 2020 (6 mo)	Retrospective	Germany, Austria, and Switzerland	85.0 (80–89)	2,678	Proximal femur	32 (26.01)	123	214 (0.61)	3,610	Inpatient
Sobti et al. [20]	March 1, 2020–May 31, 2020 (3 mo)	Prospective	UK	83.5	Not reported	Neck of femur	3 (50.0)	6	5 (10.63)	47	Inpatient
Thakrar et al. [21]	March 15, 2020–April 15, 2020 (1 mo)	Retrospective	UK	81.6 (54–100)	Not reported	Hip	4 (33.0)	12	1 (16.60)	6	30-day
Wright et al. [22]	March 11, 2020–April 30, 2020 (41 day)	Retrospective	UK	81.1 (38–98)	Not reported	Neck of femur	5 (31.25)	16	3 (16.67)	50	30-day
Zajonz et al. [23]	January 1, 2020–January 31, 2021 (1 yr)	Retrospective	Germany	82.0	219	Proximal femur	5 (41.67)	12	16 (5.35)	299	Inpatient

Values are presented as mean (range), number only, or number (%).

Table 2. Incidence of venous thromboembolism, underlying disease, complications, and length of hospital stay in COVID-19–positive and –negative groups.

Study	Total postoperative mortality	COVID-19 (+)			COVID-19 (–)			Venous thromboembolism incidence		Mean hospital stay (day)	
		Primary cause of postoperative death	Underlying disease	Complication	Primary cause of postoperative death	Underlying disease	Complication	COVID-19 (+)	COVID-19 (–)	COVID-19 (+)	COVID-19 (–)
Andrzejowski et al. [9]	8	4 Complications due to COVID-19	1 COPD 2 Diabetes 1 Lung cancer 1 Autoimmune disease 1 Prostate cancer 1 Lymphoma	Not reported	1 Pneumonia 1 t-ICH 1 Sepsis 1 Record unavailable	1 COPD 2 Diabetes 1 Lung cancer 2 Stroke 1 Hypothyroidism 1 IHD 1 Heart failure 1 CKD 1 AF	Not reported	Not reported	Not reported	Not reported	Not reported
Balakumar et al. [11]	17	5 Respiratory failures 2 Deliriums 1 Pneumonia 1 NOF fracture	Not reported	Not reported	1 Respiratory failure 1 Pneumonia 1 Old age 1 Sepsis 4 Records unavailable	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Beaven et al. [10]	30	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Clement et al. [12]	85	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Dallari et al. [13]	15	Not reported	Not reported	16 Acute anemias 6 Pneumonias 6 Other respiratory complications 3 AHFs 2 UTIs 1 ARF	Not reported	Not reported	138 Acute anemias 7 Pneumonias 8 Other respiratory complications 9 AHFs 7 UTIs 2 ARFs 3 Sepsis 2 PEs 2 Ictus cerebri 27 Other minor complications	0	2	14.7	10.9

Egol et al. [14]	7	Not reported	8 Cardiovascular diseases (excluding hypertension) 11 Hypertensions 1 Immunocompromised state 7 Diabetes 4 ARFs 9 Hyperlipidemias 6 Dementias	3 Sepsis 2 Bacterial pneumonias 10 Viral pneumonias 2 PEs 2 MIs 7 ARDSs 2 Cardiac arrests 3 ARFs 7 Anemias 7 Hypotensions 6 AFs	Not reported	40 Cardiovascular diseases (excluding hypertension) 67 Hypertensions 4 Immunocompromised states 20 Diabetes 8 ARFs 38 Hyperlipidemias 27 Dementias	3 Sepsis 1 Bacterial pneumonia 3 PEs 3 MIs 2 Strokes 2 ARDSs 8 ARFs 6 UTIs 35 Anemias 13 Hypotensions 12 AFs	2	3	9.8	5
Fisher et al. [15]	3	Not reported	Not reported	1 Cardiac arrest 5 Postoperative anemias 1 ARDS 2 PE/DVTs 2 Pneumonias 1 MI	Not reported	Not reported	1 Cardiac arrest 4 Postoperative anemias 1 ARDS 1 Pneumonia 1 Sepsis 1 UTI	2	0	9	7.91
Greensmith et al. [24]	7	2 Complications due to COVID-19	Not reported	Not reported	1 Complication from disseminated malignancy 1 UGIB 1 SUO 1 Urosepsis 1 Stroke	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Hall et al. [16]	33	9 Complications due to COVID-19	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
LeBrun et al. [17]	4	3 Complications due to COVID-19	3 Hypertensions 2 Hyperlipidemias 2 Diabetes 1 Osteoporosis 2 Dementias 1 Malignancy 1 PUD 1 GERD 1 BPH	6 Pneumonias 1 Arrhythmia 2 UTIs	1 Intraoperative cardiac arrest	1 CAD 1 AF 1 Hypertension 1 Hyperlipidemia 1 Diabetes 1 Hypothyroidism 1 CKD	5 Pneumonias 7 UTI 1 DVT 1 MI 2 Decubitus ulcers	0	1	8	6

Lim et al. [18]	8	1 Complication due to COVID-19	1 Asthma 1 Other lung disease 5 Cardiovascular diseases 3 Malignancies 2 Diabetes 3 Renal diseases 3 Dementia	Not reported	Not reported	5 Asthmas 6 COPDs 12 Other lung diseases 54 Cardiovascular diseases 30 Malignancies 14 Diabetes 19 Renal diseases 16 Dementias	Not reported	Not reported	Not reported	30.3	12
Pass et al. [19]	246	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	19.1	15.1
Sobti et al. [20]	8	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Thakrar et al. [21]	5	4 Complications due to COVID-19	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Wright et al. [22]	8	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	17	10
Zajonz et al. [23]	21	5 Complications due to COVID-19	Not reported	Not reported	7 Cardiac decompensation with myocardial failures 2 PEs 2 Pneumonias 1 MI 1 Sepsis 1 GI bleeding 1 Epileptic shock with aspiration 1 Hepatic failure	Not reported	Not reported	0	2	15.6	11.5

COPD, chronic obstructive pulmonary disease; t-ICH, traumatic intracranial hemorrhage; IHD, ischemic heart disease; CKD, chronic kidney disease; AF, atrial fibrillation; NOF, neck of femur; AHF, acute heart failure; UTI, urinary tract infection; ARF, acute renal failure; PE, pulmonary embolism; MI, myocardial infarction; ARDS, acute respiratory distress syndrome; DVT, deep vein thrombosis; UGIB, upper gastrointestinal bleeding; SUO, sepsis of unknown origin; PUD, peptic ulcer disease; GERD, gastroesophageal reflux disease; BPH, benign prostatic hyperplasia; CAD, coronary artery disease; GI, gastrointestinal;

Table 3. GRADE summary of findings

Outcome	Anticipated absolute effect[a)] (95% CI)		Relative effect OR (95% CI)	No. of participants	No. of observational studies	Certainty of the evidence (GRADE)
	Risk with COVID-19 (–) (per 100)	Risk with COVID-19 (+) (per 100)				
Overall mortality	5	30 (25–36)	7.72 (6.01–9.93)	7,452	16	Low
Postoperative mortality at inpatient	5	32 (24–41)	8.67 (5.82–12.91)	6,753	10	Low
Postoperative mortality at 30-day follow-up	8	38 (26–51)	7.32 (4.30–12.49)	699	6	Very low[b)]
Postoperative mortality in the patients with a mean age of >60 yr	5	30 (25–36)	7.75 (6.02–9.97)	7,418	15	Low
Postoperative mortality in the patients with a mean age of <60 yr	4	20 (2–76)	5.75 (0.46–72.30)	34	1	Very low[c)]
Venous thromboembolism incidence	1	4 (1–11)	4.08 (1.23–13.58)	993	5	Low

GRADE, Grading of Recommendations, Assessment, Development, and Evaluation; CI, confidence interval; OR, odds ratio.

[a)]The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). [b)]One study had a high risk of bias and two studies had moderate risk of bias. [c)]The 95% CI crosses the line of no effect and has an insufficient sample to meet the optimal information size criteria.

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