Length of hospital stay and mortality of hip fracture surgery in patients with Coronavirus disease 2019 (COVID-19) infection: A systematic review and meta-analysis

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ABSTRACT

Background:
Coronavirus disease 2019 (COVID-19) patients who undergo hip fracture surgery are expected to have worse outcomes because they are vulnerable to developing COVID-19-associated complications. The present review attempted to assess the in-hospital and 30-day mortality rates as well as the length of hospital stay in patients with COVID-19 infection who had hip fracture surgery.

Methods:
Two authors independently searched Google Scholar, PubMed, Web of Knowledge, SCOPUS, and Embase, based on the MeSH-matched scientific keywords. The nine-star Newcastle-Ottawa Scale (NOS) scoring system was employed to assess the methodological quality of all eligible studies.

Results:
Eleven cohort studies that included 336 patients comprised the study. Three studies reported in-hospital mortality. Eight studies reported 30-day postoperative mortality. The pooled in-hospital mortality rate was 29.8% (95% CI: 26.6%-35.6%). The pooled 30-day postoperative mortality rate was 35.0% (95% CI: 29.9%-40.5%). The mean hospital stay was 11.29 days (95% CI: 10.65 days-11.94 days).

Conclusions:
The rates of in-hospital and 30-day mortality in COVID-19 patients who undergo hip fracture surgery is high. These data suggest delaying hip fracture surgery until COVID-19 infection of the patients is controlled.

Level of Evidence:
Level II.

Key Words
COVID-19, hip fracture, surgery, mortality

INTRODUCTION

Coronavirus disease 2019 (COVID-19) emerged as the most important health problem at the end of 2019 becoming a life-threatening global feature and affecting almost all human societies. As of this writing, more than 40 million cases have been reported worldwide, leading to more than 1.5 million deaths associated with this pandemic,[1] and despite the measures and protocols implemented, the disease continues to take lives. Not only has it placed significant burdens on health systems but also has posed a great challenge in the management of patients, particularly in specialized centers.[2] Many physicians are confused about how to manage patients with the disease, especially in those with concurrent disorders or injuries that require medical interventions or emergency surgery. However, the question of whether surgery for these patients should be performed at the earliest opportunity or delayed remains unanswered.[3,4] Some surgeons are concerned that performing surgical interventions after COVID-19 recovery might also increase the risk of postoperative morbidity and mortality.[5] This is especially true for orthopaedic or traumatic lesions that are associated with a high probability of coagulopathy or hemorrhagic events.[6]

Hip fractures constitute a large proportion of hospital referrals, especially due to traumatic and osteoporotic-related events. Obviously, most of these fractures require emergent surgical management.[7,8] These fractures represent a health care concern, with an in-hospital, 30-day, and 1-year mortality of nearly 1.5%, 7.5%, and 25%, respectively.[9]

According to recent reports, patients with hip fractures may be more vulnerable to COVID-19 complications since a considerable number of patients are elderly (>65 yr of age) and have several underlying comorbidities such as hypertension, diabetes, and cardiovascular disorders. This is even more prominent in developing countries with a

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fundamental shortage of hospital services and patient admissions.[10,11] In fact, it is expected that patients with hip fractures will face twice as many problems during COVID-19 as in previous periods without the pandemic, both in terms of hospital admission limitations and postoperative outcomes.[12,13]

An in-depth knowledge of the mortality rate of hip fracture surgery in COVID-19-infected patients is required to answer whether this surgery should be performed at the earliest opportunity or to delayed it as much as possible. The present review attempted to systematically assess the in-hospital and 30-day mortality rates of hip fracture surgery in patients infected with COVID-19. The authors hypothesized that with a high mortality rate in patients with COVID-19 who underwent surgery for hip fracture, these surgeries could be delayed until resolution of the COVID-19 infection.

MATERIALS AND METHODS

Ethical Review

Institutional review board approval is not required for systematic reviews or metaanalyses.

Literature Search

The current meta-analyses followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline.[14] Two authors (HT and MH) independently assessed all manuscripts indexed in the international journals databases, including Google Scholar, PubMed, Web of Knowledge, SCOPUS, and Embase up to October 2020. The used MeSH-matched scientific keywords were "Hip," OR "fracture," OR "COVID-19," OR, "surgery," OR "outcome," OR "orthopedic." The details of the search strategy and final selection of the eligible studies are shown in Figure 1.

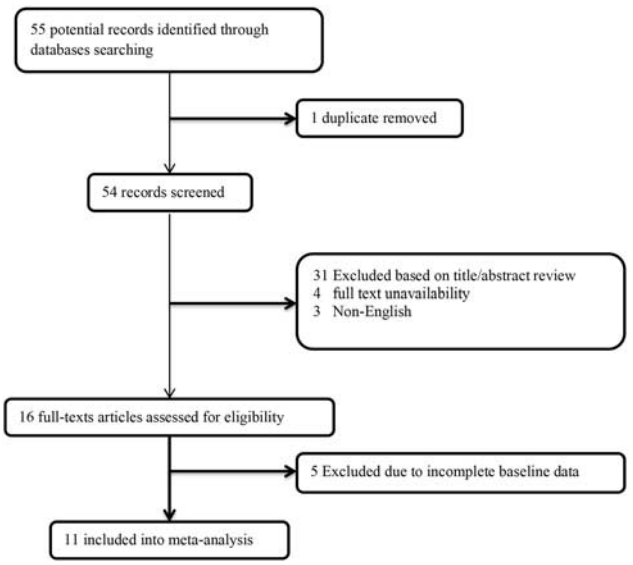

FIGURE 1. The flowchart of screening the eligible studies.

Study Selection

The following criteria were considered for selecting the studies for initial assessment: (1) original longitudinal (prospective or retrospective cohort) studies enrolling COVID-19 patients undergoing hip fracture surgery, and (2) the studies that assessed and compared early and/or long-term procedural outcome. In this regard, the case reports, case series, or review studies were excluded from the analysis.

Data Extraction and Quality Assessment

Two authors independently extracted the data and evaluated the study quality (M.H. and S.F.). Any disagreement between the two authors was resolved by discussing with the third author (A.A.). In addition to outcome-related information, authors' names, year of publication, numbers of patients included with gender and age distribution, and follow-ups also were extracted. The nine-star Newcastle-Ottawa Scale (NOS) scoring system was employed to assess the methodological quality of all eligible studies. In this respect, each study was assessed qualitatively for the three criteria of (1) the selection of the study groups, (2) the comparability of study groups, and (3) the ascertainment of the outcome. Studies awarded seven stars or more were deemed to be high quality.[15]

Primary and Secondary Outcomes

The primary outcome of the study was to assess the pooled rate of mortality for in-hospital and 30-day follow-up. The secondary outcome was the overall mean length of hospital stay.

Statistical Analysis

The multivariable-adjusted risk estimate was pooled for the presence or absence of each post-procedural outcome and mentioned as hazard ratio (95% confidence interval). The fixed-effects model also was used to obtain the pooled dichotomous data using the mean difference (MD) followed by reporting 95% CIs and its related corresponding *P* values for assessing the difference in the mean hospital stay. Heterogeneity among studies was assessed using the Cochrane Q statistic ($P < 0.10$, statistically significant heterogeneity) and the I^2 statistic ($\geq 50\%$, statistically significant heterogeneity). In this regard, the fixed-effect model was used for insignificant heterogeneity; otherwise, the random effect model was used. The Egger's test was employed to determine publication bias, with a *P*-value < 0.10 suggesting statistical significance. All statistical analyses were done using the Comprehensive Meta-analysis software (Biostat, Englewood, NJ).

RESULTS

Study Selection and Quality Assessment

The flow diagram of the study selection process is presented in Figure 1. Eleven articles were included in the analysis.[16–26] Table 1 describes the baseline characteristics of the included studies. The quality assessment showed a NOS score of 7 or higher for all studies, indicating the high methodological quality of all studies (Table 2).

TABLE 1. Characteristics of the included studies

References, Country	Number of patients	Mean age	Male/ female	COVID-19 positive stage	Anesthesia	DVT prophylaxis	Mean time to surgery (hours)	Follow-up time
Cheung and Forsh, USA[16]	10	71.4	2/8	Positive testing	General or spinal	NA	28.8	In-hospital
De *et al.*, UK[17]	34	85.9	12/22	Positive testing & symptoms	General or spinal	Yes	49.6	30 days
Egol *et al.* USA[18]	17	82.4	12/5	Positive testing	General or spinal	Yes	64.8	30 days
Hall *et al.*, UK[19]	27	83.6	14/13	Positive testing or symptoms	General or spinal	NA		30 days
Kayani *et al.* UK[20]	82	71.9	31/51	Positive testing & symptoms	General or spinal	NA	36.0	30 days
Konda *et al.*, USA[21]	31	81.6	14/17	Positive testing or symptoms	NA	NA		30 days
LeBrun *et al.*, USA[22]	9	86.5	3/6	Positive testing	General or spinal	NA		In-hospital
Muse *et al.*, USA[23]	5	79.0	1/4	Positive testing	General or spinal	Yes	48.0	In-hospital
Narang *et al.*, UK[24]	86	86.0	33/53	Positive testing & symptoms	NA	NA		30 days
Thakrar *et al.*, UK[25]	12	81.6	4/8	Positive testing & symptoms	NA	NA	51.2	30 days
Vives *et al.*, Spain[26]	23	89.2	10/13	Positive testing	NA	NA	38.4	30 days

COVID-19, coronavirus disease 2019; DVT, deep vein thrombosis; NA, Not available; UK, United Kingdom; USA, United States of America.

TABLE 2. The quality assessment of the studies according to the nine-star Newcastle-Ottawa scale (NOS) scoring system

References	Selection				Comparability		Outcome			Total
	❶	❷	❸	❹	❺	❻	❼	❽	❾	
Cheung and Forsh,[16]	★	★	★		★	★	★	★	★	8
De *et al.*,[17]	★	★	★	★	★	★	★	★		8
Egol *et al.*,[18]	★	★	★	★	★	★	★	★		8
Hall *et al.*,[19]	★	★	★	★	★	★	★	★	★	8
Kayani *et al.*,[20]	★	★	★		★	★	★	★	★	8
Konda *et al.*,[21]	★	★	★	★	★	★	★	★		8
LeBrun *et al.*,[22]	★	★	★	★		★	★	★		7
Muse *et al.*,[23]	★	★	★	★	★	★	★	★	★	8
Narang *et al.*,[24]	★	★	★	★	★	★	★	★	★	8
Thakrar *et al.*,[25]	★	★	★	★		★	★	★		7
Vives *et al.*,[26]	★	★	★	★		★	★	★		7

TABLE 3. Postoperative death and length of hospital stay

References, Country	Death	LOS (days)
Cheung and Forsh, USA[16]	In-hospital: 1/10	7.8 ± 4.4
De *et al.*, UK[17]	30-day: 14/34	21.4 ± 11.5
Egol *et al.*, USA[18]	In-hospital: 6/17 30-day: 9/17	9.8 ± 5.2
Hall *et al.*, UK[19]	30-day: 9/27	
Kayani *et al.*, UK[20]	30 days: 25/82	13.8 ± 4.6
Konda *et al.*, USA[21]	In-hospital: 7/31 30-day: 11/31	8.9 ± 6.8
LeBrun *et al.*, USA[22]	In-hospital: 5/9	8.0 ± 2.0
Muse *et al.*, USA[23]	In-hospital: 0/5	10.8 ± 2.2
Narang *et al.*, UK[24]	30-day: 30/86	
Thakrar *et al.*, UK[25]	30-day: 4/12	
Vives *et al.*, Spain[26]	30-day: 7/23	

LOS, length of stay; UK, United Kingdom; USA, United States of America.

Characteristics of the Study Population

All 11 eligible studies were designed as cohort studies; the follow-up time ranged from inpatient (3 studies) to 30 days (8 studies). The study population included a total of 336 patients who had a positive test for COVID-19 and underwent hip fracture surgery of various types. The patients were between the age of 71.4 to 89.2 yr (Table 1).

Early and Late Mortality

The number of postoperative deaths in each study is demonstrated in Table 3. Analyzing the in-hospital mortality rate showed a pooled death rate of 29.8% (95% CI: 26.6% to 35.6%). The pooled 30-day postoperative death was 35.0% (95% CI: 29.9% to 40.5%). The heterogeneity across the studies in assessing in-hospital and 30-day mortality were not significant with I^2 values of 40.777 ($P = 0.149$) and 0.000 ($P = 0.796$), respectively (Figures 2 and 3). The Egger test also detected nonsignificant publication bias for all assessments ($P = 0.573$, $P = 0.601$, respectively).

The Length of Hospital Stay

The mean hospital stay of the patients was 11.29 days (95% CI: 10.65 to 11.94 days). However, the heterogeneity across the studies in the pointed measurements was significantly relevant, with the I^2 value of 93.088 ($P < 0.001$). Egger test detected no significant publication bias ($P = 0.573$).

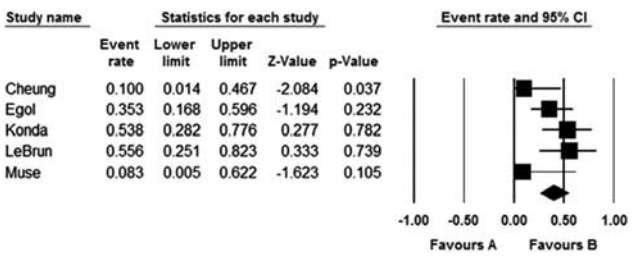

FIGURE 2. The pooled analysis of in-hospital death rate in hip-fracture surgery in COVID-19 patients.

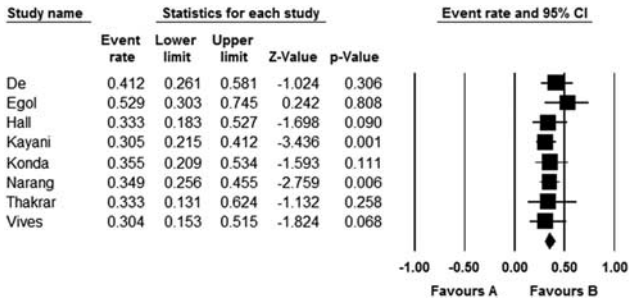

FIGURE 3. The pooled analysis of 30-day death rate in hip-fracture surgery in COVID-19 patients.

DISCUSSION

In this review the authors evaluated the impact of COVID-19 infection on the mortality rate of patients undergoing hip fracture surgery, as well as the length of hospital stay. According to these results, the in-hospital and 30-day mortality rates were 29.8% and 35%, respectively. The mean length of hospital stay was 11.29 days. According to these results, delaying hip fracture surgery until resolution of the COVID-19 infection was recommended to reduce the rate of postoperative mortality.

Mortality of hip fracture surgery is attributed to a variety of factors, including the presence of shock, dialysis, obesity, time to surgery, and comorbid disorders.[27] For this reason, the mortality rate of hip fractures varies between the studies. Groff *et al.*[28] reported an in-hospital mortality rate of 3% (75/2464) in a retrospective study of consecutive patients older than 65 yr of age who were treated for a hip fracture at two institutions in the USA. Sanz-Reig *et al.*[29] reported an in-hospital mortality rate of 11.4% in 331 Spanish patients older than 65 yr of age with hip fracture. Erickson *et al.*[30] searched the PearlDiver database of Medicare patients with the diagnostic codes for femoral neck fractures and related conditions. During a 5-year period (2005 to 2010), 751,232 femoral neck fractures were recorded, with 11,420 deaths during the initial hospital stay. Accordingly, an overall mortality rate of 1.5 was reported, which was in men almost twice that of women. In addition, patients older than 84 yr of age had a higher risk of death after sustaining a femoral neck fracture.[30] In the present review, the in-hospital mortality rate of hip fracture of 29.8% in this study was markedly higher than earlier reports. This result revealed the significant adverse impact of COVID-19 infection on the outcome of hip-fracture surgery.

Tsang *et al.*[31] reported a 30-day mortality rate of 5.36% after hip-fracture surgery in England, Wales, and Northern Ireland. In a study by Daugaard *et al.*[32] the 30-day mortality rate was 10% in 38,020 Danish patients. In the study of Carretta *et al.*[33] the 30-day mortality rate of postoperative hip fracture surgery was 3.5% in 1320 Italian patients. The 30-day mortality rate of hip fracture was 1.4% in 874 South Korean patients, reported by Choi *et al.*[34] In spite of the considerable heterogeneity among the mortality rates of earlier studies, it barely exceeds 10%. However, the 30-day mortality rate of hip fracture was 35% in the present analysis. This result reveals a significantly increased mortality in COVID-19 patients undergoing surgery for a hip fracture.

Lim and Pranata[35] in 2020 conducted a systematic review and meta-analysis to measure the impact of COVID-19 infection on

mortality in patients with hip fracture. Six studies recruiting 984 participants were included in that analysis. Based on their results, the death rate in patients with simultaneous hip fracture and COVID-19 was considerably higher than in hip fracture without COVID-19 (36.0% vs. 2.0%). They did not separately report the in-hospital and 30-day mortality rates. However, the obtained rate of mortality was similar to our study.

The mean hospitalization period of COVID-19 patients who underwent surgery for hip fracture was 13.2 days in the study of Lim *et al.*[35] The mean length of hospitalization was 11.29 days in the present study. The mean length of hospital stay for hip fracture surgery was 15.7 days in the study of Tan *et al.*,[36] 19.6 days in the study of Lavikainen *et al.*,[37] 30.7 days in the study of Yoo *et al.*,[38] and 30.8 days in the study of Ireland *et al.*[39] Comparing the length of hospital stays before and after the COVID-19 pandemic reveals a shortened hospitalization period after the COVID-19 outbreak probably to prevent transmission of the virus to the medical staff and other hospitalized patients. The reduced length of hospitalization could also affect the outcome of patients and requires investigation in future studies.

Several underlying factors could impact the mortality of COVID-19 in patients undergoing surgery for hip fracture, including the high frequency of women and the old age of patients. The presence of underlying comorbidities such as diabetes, hypertension, and cardiovascular disease can increase the mortality rate of patients.[13,17,18] Trauma and surgical interventions also affect the outcome of COVID-19. It is well demonstrated that skeletal injuries and related surgical procedures create certain pathological conditions such as activating inflammation cascades and subsequent release of inflammatory cytokines, which strengthen COVID-19-induced inflammation, possibly leading to cytokine storm.[40] Such pathological processes may lead to COVID-19-related life-threatening events such as respiratory failure, kidney dysfunction, and cardiovascular events.[41] Therefore, hip-fracture surgery in patients with COVID-19 infection should be delayed as much as possible, perhaps until the COVID-19 infection of patients has been adequately controlled.

Limitations and Future Study Perspectives

This study was not without limitations. The included studies were heterogeneous in several aspects that could have affected the rate of mortality. For instance, some studies included patients based on their positive COVID-19 testing, regardless of their symptoms, whereas others only included symptomatic patients with positive COVID-19 testing. The type of anesthesia was also heterogenous so that a combination of general and spinal anesthesia was included in the majority of, while it is accepted that the rate of mortality for hip fracture is higher with general anesthesia.[42] Deep vein thrombosis prophylaxis and type of anticoagulant also could be regarded as a source of heterogeneity, which was not provided in most of the included studies. The timing of the surgery also was different between the studies and could be considered a condoning factor as delay to surgery beyond 24 hr has been clearly shown to increase mortality risk.[43] Future studies should clarify how the severity of COVID-19 symptoms affects decision-making regarding surgical treatment and how length of hospital stays affect patient outcomes after surgery for hip fracture.

CONCLUSIONS

Concomitant COVID-19 infection significantly increases the in-hospital and 30-day mortality in patients who undergo hip fracture surgery. These results suggest postponing the hip-fracture surgeries in patients with COVID-19 infection, who are already venerable to COVID-19 death caused by several underlying conditions. Since this specific group of patients often is highly medically unstable, the new conventional wisdom of expedited surgery needs modification, with surgery being deferred until medical optimization has been achieved. Individualizing the decision for surgery based on the severity of COVID-19 symptoms and other patient risk factors could be regarded as another strategy to reduce the rate of mortality, which needs further clarification in future studies.

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