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Management of hip fracture in COVID-19 infected patients

Qin HC *et al.* HF with COVID-19

Abstract

Given that the global population of the elderly is expanding and the difficulty of recovery, hip fractures will be sure to transform into a big challenge and a critical health issue for all of humanity. Even though people have been suggested to spend more time at home during the coronavirus disease 2019 (COVID-19) pandemic, hip fractures show no sign of abating. Extensive studies have shown that hip fracture patients with COVID-19 infection have a multifold increase in mortality compared to those uninfected and a more complex clinical condition. At present, no detailed research has systematically analyzed the relationship between these two conditions and proposed a comprehensive solution. This paper aims to systematically review the impact of COVID-19 on hip fracture and provide practical suggestions. We found that hip fracture patients with COVID-19 endure higher mortality rates and more complicated clinical outcomes. Indirectly, COVID-19 somewhat prevents hip fracture patients from receiving regular medical treatment. Regarding the problems we encounter, we provide clinical recommendations based on existing research evidence and a clinical flowchart for the management of hip fracture patients with COVID-19 positive. Our study will help clinicians prepare adequately in advance when dealing with such patients and optimize treatment decisions.

INTRODUCTION

Hip fracture has been recognized as a worldwide health problem, the incidence of hip fractures is on the rise due to an aging population^[1]. Hip fractures are expected to grow from 258000 per year in 2010 to 458000 per year in 2050 in the United States. By 2050, the global number of hip fractures is expected to reach 4.5 million per year^[2]. Older patients endure more medical comorbidities, making it harder for them to recover from hip fractures^[3]. Given that the global population of the elderly is expanding and the difficulty of recovery, hip fractures will be sure to transform into a big challenge and a critical health issue for all of humanity. The new coronavirus disease-2019 (COVID-19) has posed a substantial threat to people's social lives and medical health care throughout the world. The Centers for Disease Control and Prevention in the United States reported 33.8 million confirmed COVID-19 cases and 605905 related fatalities as of July 2021. COVID-19 has had a significant impact on hospital and intensive care unit (ICU) expenditures as well as the length of stay^[4]. The virus is transmitted by droplets and causes a flu-like upper respiratory infection with symptoms such as coughing, fever, and dyspnea in severe instances^[5]. However, to control the spread of the disease, the implementation of epidemic prevention policies, lockdown of social activities, and travel restrictions have reduced traumatic injuries admissions to an all-time low. The mechanism of trauma-related fractures shifts from high energy to low energy, for instance, emergency admissions for falls from great heights and vehicle accidents have declined^[6]. Most of the cases seen were from stumbles and falls from a standing position, particularly in elderly individuals with osteoporosis. Therefore, hip fractures in the elderly are still being seen generally at an unchanged rate, especially the fragility fractures around the hip like neck femur and intertrochanteric fractures^[7,8]. In this vulnerable group, a significant number of patients were at a risk for infecting COVID-19, as higher ages always with weaker immune systems, more chronic illness, and poorer tolerance^[9]. The virus has been found to not only damage the respiratory system

but affect multiple organ systems. So, it is a tricky challenge for medical practitioners to solve when two conditions exist in the same person, especially the elderly^[10].

Hip fracture patients defined as COVID-19 positive, whether preoperatively or postoperatively infected, have a multi-systemic impact that makes perioperative care, the course of surgery, and postoperative rehabilitation more difficult and complex. Compared to uninfected patients, they are exposed to more risks. Recent studies have identified that COVID-19 positive status is an independent predictor of mortality in hip fracture patients^[11]. The data collected by Wang *et al*^[12] demonstrated The relative risk for postoperative mortality in COVID-19 positive patients compared to uninfected was 5.66 (95% CI: 4.01-7.98; $P < 0.001$). In a retrospective multicenter assessment, Oputa *et al*^[13] discovered that the mortality of COVID-19 positive hip fracture patients at 120 d had also increased dramatically (63%:17%, $P < 0.01$). Apart from that, COVID-19 positive patients are associated with increased length of hospital stay, more admissions to the critical care unit, higher risk of perioperative complications compared^[14].

Though the prevention of COVID-19 has become a part of daily life for people all over the world and the virus does place a huge burden on both patient conditions and medical systems, the corresponding coping strategies are constantly being updated. To address these new-rising challenges, increased attention to this comorbidity is necessary not only to gain a thorough understanding of the clinical condition of COVID-19 positive patients but also to provide optimal clinical treatment options for the patient. Here, we performed a narrative review to (1) Provide an overview of the clinical impact in COVID-19 positive hip fractures compared to those diagnosed negative. Provide clinicians with predictability so that they can fully prepare in advance; and (2) Provide practical suggestions regarding existing diagnosis and care methods to overcome various difficulties caused by COVID-19 infection.

1 IMPACT OF COVID-19 ON PATIENTS WITH HIP FRACTURES

The direct impact of COVID-19 itself, as well as quarantine methods against the COVID-19, both have a significant influence on the diagnosis and treatment of hip fracture

patients. Since the age distribution of patients with hip fractures is mainly over 60 years old, most of them will experience multiple complications and cannot completely reclaim their pre-injured physical function^[15]. Therefore, if they are further infected with COVID-19, the underlying medical comorbidities, severity of COVID-19 complications, corresponding treatment measures and combined morbidity and mortality of the two conditions remain a mystery.

² Acute respiratory distress syndrome (ARDS) with widespread alveolar damage, diffuse thrombotic alveolar microvascular occlusion, and inflammatory mediator-associated airway inflammation are three ways how the virus harms the lungs histologically. The patient clinically presented with dyspnea decreased oxygen saturation, even pulmonary embolism^[16]. A significant increase in mortality in patients with COVID-19 and hip fractures has been extensively documented^[17-20]. According to recent research, hip fractures with COVID-19 positive are vulnerable to experience ⁵ complex perioperative complications, such as acute sarcopenia, sepsis, pneumonia, acute respiratory failure, cardiac arrest, and acute kidney injury than patients with COVID-19 negative^[21-23], more likely to experience life-threatening complications, such as acute respiratory failure, cardiac arrest, and serious infections^[24,25]. These perioperative complications present challenges to surgery. Some complications of certain systems that may affect the long-term recovery of hip fracture patients. For example, COVID-19 infection can cause muscle atrophy in several ways, then muscle atrophy will lead to significant detriments in physical function, lead to increased risk of falls^[23]. After the operation, since virus-self can introduce a widespread hyperinflammatory state (a cytokine storm), this condition is further exacerbated by the operation and lead to widespread organ failure. In addition, both diseases can also cause a procoagulant state and increase the rate of thromboembolic events^[26]. Complex clinical symptoms require extra precise therapeutic intervention and support, as well as a longer length of stay^[27]. Prolonged length of stay may be due to barriers to discharge planning, including awaiting COVID-19 positive patients to become negative. ⁴ COVID-19 positive patients are also more likely to be admitted to the ICU care unit, require

ventilators and other medical support equipment after surgery. Since the COVID-19 infection mainly affects the lungs, causing symptoms such as dyspnea and decreased oxygen saturation, making ventilator a necessary auxiliary therapeutic instrument for such patients.

In addition to the acute phase, COVID-19 also causes many long-term, multi-system sequelae, which could greatly delay the rehabilitation process of hip fracture. Because the COVID-19 pandemic lasts less than a year, it is difficult to identify and investigate its long-term sequelae. However, follow-up of patients who recovered from severe acute respiratory syndrome coronavirus 1 (SARS-COV-1) infection in 2003 reported some results that may explain the long-term prognosis of SARS-COV-2 infection. According to a follow-up study of SARS-CoV-1 survivors, the pulmonary ventilation performance of all patients was affected to varying degrees, and the pulmonary diffusion function in more than one-third of patients was considerably damaged^[28,29], ultimately hindering the patient's daily life. In addition to respiratory sequelae, such as Alzheimer's Disease, Parkinson Disease, and Multiple Sclerosis of the nervous system^[16], acute sarcopenia of the muscular system, all are molecularly associated with COVID-19 infection and pose bad effects on hip fractures.

From an indirect point of view, as the COVID-19 pandemic has led to a global surge in critically ill patients, hospitals have been forced to reallocation resources into virus screening for patients' admission, setting up special isolation corridors, wards, and ORs (operating rooms), which potentially reducing patients' access to emergency care^[30]. For positive or suspected patients requiring emergency hip surgery, multiple admission screening, and evaluation, waiting for a designated negative pressure OR will inevitably delay operation time^[31]. Post-operatively, As the patient is in the isolation ward, nurses, rehabilitation therapists and physicians have less access to them, resulting in the absence of routine in-hospital care. After discharge, they are suggested to keep at home. In order to minimize the number of visits to the hospital and reduce the risk of re-infection, frequent follow-up visits will not be recommended, which increases the difficulty of long-term postoperative recovery^[32].

In conclusion, Not only is the virus-self posing a severe impact on patients, but some mandatory adoptions in response to COVID-19 are also potentially having an indirect impact on patients. (Effects of COVID-19 on patients with hip fracture are presented in Figure 1).

MANAGEMENT TO ADDRESS THE ISSUE

Admission screening

With no definitive treatment to date, prevention is critical. To reduce infection between positive patients and other patients and hospital staff, patients admitted to the hospital and accompanying family members must be screened. Diagnosis of COVID-19 patients must be based on epidemiological history, clinical symptoms, radiology test, and most importantly, a reverse-transcription PCR of nasopharyngeal and oropharyngeal swab samples^[33]. An epidemiological inquiry should be deployed first to determine whether the patient has any contact with close contact (someone who has clearly had contact with an infected person, possibly an asymptomatic carrier of the virus), an infected person, or high-risk communities in the past 14 d.

Second, diagnostic evidence is further provided by the typical clinical features of COVID-19 infection, including fever, dry cough, and lung imaging features. Blood indicators can also be used as diagnostic indicators, such as white blood cell count, platelet count^[34].

However, 4%-18% of COVID-19 positive patients are asymptomatic carriers of the virus, and the incubation period for COVID-19 is 10 to 14 d, during which the disease is highly contagious, but the patient may not show characteristics of systemic infection. Therefore, we strongly recommend nucleic acid testing for all hospitalized patients and multiple nucleic acid tests for patients with relevant clinical symptoms and patients with suspected epidemiology within 14 d.

Patient triage (determination of treatment)

It has been widely received that early surgery should be performed in elderly patients with hip fractures^[35]. If the condition does not allow the surgery to be performed and the waiting time for surgery is prolonged, there are many complications associated with prolonged bed rest, such as ⁶respiratory failure, urinary, and genital tract infection, stones, bedsores, body temperature disorders, deep vein thrombosis, ultimately affecting the recovery of physical functions^[36]. However, COVID-19 patient status should play a role in determining the timing of surgery^[37]. Recent studies have suggested that mortality in patients with COVID-19 positive may be due to virus-driven high inflammation. Significantly elevated levels of multiple inflammatory markers can lead to widespread organ failure. At the same time, inflammation from acute fractures or fracture repair surgery may further exacerbate the status of patients with acute COVID-19 infection. Therefore, surgical thresholds for positive patients should be higher than normal patients, particularly in the advanced-age group. Greater consideration should be given to the possibility of postponing non-emergency procedures and promoting non-surgical treatment. We recommend surgery only for patients ⁸with asymptomatic or mild COVID-19 symptoms. Though they may have temporarily increased oxygen demands postoperatively, they can safely undergo early surgical intervention after appropriate medical optimization^[38]. But we still suggest that if an emergency operation is required, a comprehensive preoperative understanding of the patient's multi-system clinical data and a multidisciplinary group of experts should be established to determine the optimum moment of surgery^[39]. Minimally invasive surgery, which requires less surgical time and minimizes blood loss, is also recommended for older patients with hip fractures. Conservative treatment with traction may be considered for high-risk COVID-19 patients with hip fractures.

Preoperative and intraoperative matters needing attention

Rigorous quarantine measures should be immediately followed by the admission of COVID-19 positive patients. It is necessary to rationally design the hospital passage for infected and non-infected, as well as the isolation wards. To prevent cross-infection, the

infected are sent to an isolation ward, where separate teams should be appointed. Set up a channel for the transfer of COVID-19 patients, but only if the transfer is minimal in the hospital. The suspected will be assigned to a separate room until multiple nucleic acid test results are obtained before further treatment. Medical institutions with limited medical technology and resources are advised to transfer patients to special hospitals equipped to treat COVID-19 patients.

The management of special passage, OR, and isolation ward are strict during the pandemic, which leads to the delay of the operation start time, the extension of operation duration, the difficulty of prognosis observation, and the difficulty of multi-disciplinary intervention such as postoperative rehabilitation intervention. Yu *et al*^[31] found that the waiting time for surgery in the outbreak period is longer due to mandatory COVID-19 screening. Early surgical intervention can improve patient outcomes. On the contrary, prolonged operation time will increase the incidence of complications. Patients who are determined for emergency surgery should be prepared with as little time as possible and reduce the waiting time for patients who meet surgical criteria. About the choice of anesthesia and surgical procedure, there are still no guidelines for hip fractures with COVID-19 hip to help them decide which procedure is the best option. ⁹ Spinal anesthesia for hip-fracture surgery in older adults was not superior to general anesthesia with respect to survival and recovery of ambulation^[40]. And type of surgery affects hospital length of stay. Open reduction and internal fixation, and closed reduction and percutaneous pinning lead to fewer in-patient days than total hip arthroplasty and hemiarthroplasty, which should be taken into consideration in anesthesia and surgical method^[41].

Designated isolation ORs and surgical instruments should be prepared in advance, and cancellation of elective theatres can be advocated to offset increased waiting time for surgery^[42]. In addition, there should be strict standards in the OR. The majority of ORs are under positive pressure. In these circumstances, a specialized OR should be set up with negative pressure. ⁷ The number of people in the OR must be reduced to the strict minimum and entering and leaving times of room should be avoided as much as ⁷

possible during surgery. Disposable equipment is preferred^[43]. Once the surgery is done, thorough disinfection of the OR is imperative for the next operation. Regardless symptomatic or not, all patients require interval testing with further swabs following surgery^[44].

Efforts should be made to coordinate Intra-departmental allocation and redeployment of human resources in this pandemic. The existing model should be updated to neutralize the impact of COVID-19.

Postoperative care

Postoperative care involves multiple dimensions. ⁶ Supportive and nutritional treatment should be prioritized after the operation and individualized treatment should be tailored to each patient's specific situation. A multicenter observational cohort study from Rasidovic demonstrated that male sex, smoking, and patients with two or more comorbidities (e.g. diabetes, dementia) were associated with higher mortality rates^[45]. Extracapsular fractures are also an indicator of high mortality^[46]. Smoking, alcohol consumption, and attitudes to COVID-19 may explain the higher prevalence in men than women^[47]. So, it is clinically meaningful to strengthen the post-operative care of males, smokers, drinkers, and patients with extracapsular fractures or multiple comorbidities. Multidisciplinary intervention in postoperative care should be provided by an expert team established preoperatively until the patient's clinical symptoms stabilize.

¹ Despite being a respiratory illness, COVID-19 is found to increase the risk of venous and arterial thromboembolic events^[48]. The inflammatory changes in coronavirus infectious disease-19 include a prothrombotic state with high risks of venous thromboembolism^[49]. Surgery for hip fractures may further aggravate this pathology. Therefore, postoperative use of anticoagulant drugs is necessary. Psychologically, patients under contact protection are less visited by family members and medical staff, which, together with the psychological impact of a hip fracture, leads to higher rates of anxiety, depression, and delirium^[50].

Due to lockdown, people continuously remain at home when they are discharged from the hospital. This highlights the importance of fall prevention strategies for the elderly at home. Patients at high risk of falling as indicated by the Morse Fall Scale or Berg Balance Scale before discharge are advised to wear a hip orthosis or explain the use of crutches. Indoor factors that may contribute to falls must also be corrected^[51]. Besides, the unchanging living environment and facilities at home are not conducive to the progress of patients' physical function. The benefits of physical therapy should be properly explained to patients to avoid fragility fractures. Patients are advised to engage in low-intensity aerobic exercise (e.g. indoor walking for 30 min or more per day) to strengthen muscle and balance functions. Similarly, patients with muscle atrophy should be trained in a progressive manner, and patients with previous fragility fractures significantly increased the risk of dysmotility syndrome and skeletal muscle function deficit that might presumably increase the risk of a new incident fracture^[52]. Adequate daily calcium intake and regular calcium density checks should be emphasized in the old female patient. As hospitals remain high-risk areas for COVID-19 infection, post-surgery follow-up and rehabilitation plan updates can be consulted *via* smartphone apps and telemedicine facilities, avoiding in-person visits and suddenly suspend of medical institutions^[53].

With the rapid spread of COVID-19, access to safe and effective vaccines is critical to ending the COVID-19 pandemic. Studies have shown that among hospitalized patients infected with COVID-19, despite receiving only one dose of the vaccine, mortality rates are significantly lower and hospital courses are simpler in the vaccinated group^[54]. Although vaccination entails certain risks for the elderly population, especially those with underlying medical conditions and frailty, studies continue to show that the benefits of vaccination far outweigh the potential risks for the frail elderly (e.g. long-term care facilities)^[55]. Thus, I believe it's necessary to vaccinate patients with hip fractures.

CONCLUSION

COVID-19 infections can have great adverse effects on patients with hip fractures, both directly and indirectly. However, the impact can be effectively reduced by monitoring all aspects of the post-admission process.

In this minireview, we outline the direct physiological consequences introduced by COVID-19 infection, as well as the practical issues that arise throughout the therapy and diagnosis procedure. By understanding these potential concerns in advance, staff in associated departments will be capable of making rational decisions and acquiring a comprehensive aspect of the progression of the disease. In the following part of the article, we summarize the existing experimental evidence and offer a set of optimized suggestions to improve patient outcomes. The model consists of admission screening, patient triage (determination of treatment), preoperative and intraoperative matters needing attention, and postoperative care (The clinical flow chart is presented in Figure 2). However, these recommendations are not the solution for any situation. As the prevalence of the epidemic varies across the nations, as does the medical capacity of hospitals, certain studies are required to reach a consensus that could suit more regions and circumstances. Notably, suggestive managements presented above apply not just to COVID-19 now, but also to any future highly contagious respiratory illnesses. Although the epidemic in China is now firmly under control, thanks to the government's attention, we should not be complacent, as the emergence of new and extremely contagious strains of COVID-19, such as Delta and Omicron, could make another outbreak possible. In addition, there are still certain countries in the world where suppression of COVID-19 is not ideal. Thus, the research regarding COVID-19 co-morbidity in the hip fracture is expected to continue. In the context of COVID-19 ramping wildly, it is imperative to optimize treatment strategies to turn the tables globally.

Fighting the COVID-19 pandemic has become a regular part of our lives, as well as a mountain that healthcare providers must overcome. Elderly people account for a large proportion of COVID-19 mortality^[56,57] as they are observed with more comorbidities and more fragile. Prevention and care for this subgroup are urgent, and when

combined with a life-threatening trauma, there is undoubtedly a huge strain on their clinical outcomes of them. We believe that it is necessary to form a multidisciplinary expert panel. It can not only comprehensively evaluate the timing of surgery for patients, but also provide a reasonable multidisciplinary treatment plan after surgery.

PERSPECTIVE

At present, there is limited information on their perioperative risk of increased mortality in patients who require urgent hip fracture surgery and are infected with COVID-19. Konda *et al*^[58] utilized ³ Score for Trauma Triage in the Geriatric and Middle-Aged, which is originally a tool to predict postoperative in-hospital mortality in trauma patients, to create a research-based strategy for operative vs. nonoperative management of patients with COVID-19 positive/suspected hip fractures. In subsequent research, we strongly suggest that if more experiments could further refine this risk assessment form into a more comprehensive and adaptable one. The assessment may include the patient's respiratory symptoms and fracture severity rating (which should be given primary weight), presence of complications, inflammatory indicators (such as C-reactive protein, procalcitonin, lactates), clinical scores (*e.g.*, American Society of Anesthesiologists grade, Alvarado score, sequential organ failure assessment score), smoking status, *etc.* The usage of this form could offer surgeons, physicians, and other healthcare practitioners with relevant clinical information, helping them make standardized therapeutic decisions by foreseeing potential outcomes. It has been reported that patients with asymptomatic infection or with only mild symptoms show a lower risk of perioperative morbidity and mortality associated with operations. Therefore, the surgical risk assessment for such patients should be reconsidered from that for patients with symptomatic infection^[59]. However, there are no cohort studies to prove the effect of asymptomatic infection on surgical or prognostic recovery of hip fracture. Subsequent studies should identify the criteria for assessing surgical risk in these patients and whether asymptomatic infection have an impact on hip fracture outcomes, and if so, what impact.

Besides, as COVID-19 is a severe acute respiratory infection disease^[60], most of the articles put their emphasis on the short-term clinical impact caused by it. However, as we all know, hip fracture patient requires regularly sustained rehabilitation^[61]. Currently available experimental data does not assist us to comprehend the influence of COVID-19 infection on the recovery process of hip fracture in long term. According to the report by McDonald^[62], one of the sequelae that can occur in COVID-19 patients, especially in those who develop ARDS during infection, is pulmonary fibrosis. Pulmonary fibrosis results from the excessive deposition of extracellular matrix molecules such as collagen, laminin, and fibronectin in the lung parenchyma. Eventually, the efficiency of gas exchange decreases due to thickened alveolar membrane. Patients will suffer from decreased lung function and exercise intolerance, fatigue, and dyspnea, which severely delay the restoration process compared to those who possess fully functional lungs. It is critical ² to make early predictions of the possible long-term sequelae of COVID-19 and to formulate appropriate prevention and intervention strategies. Whether continuous low-intensity physical therapy combined with cardiopulmonary breathing training can better facilitate patients reclaiming their prior functions deserves further investigation.

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Figure Legends

Figure 1 Summary of the impact of coronavirus disease 2019 positive on patients with hip fracture. ICU: Intensive care unit.

Figure 2 Clinical flow of treating coronavirus disease 2019 positive hip fractures. COVID-19: Coronavirus disease 2019.

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