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In-hospital mortality among patients with proximal femur fractures infected with COVID-19

ARTUR FALEK, SZYMON SKWARCZ, MAREK PAZDZIOR

Department of Trauma and Orthopedic Surgery and Spine Surgery, Independent Public Healthcare, Puławy, Poland

Corresponding author: Artur Falek, M.D., Ph.D.Department of Trauma and Orthopedic Surgery and Spine Surgery, Independent Public Healthcare
ul. Józefa Bema 1, 24-100 Puławy, PolandPhone: +48 81 45 02 152; E-mail: ortopedia.bema1@gmail.com

Abstract: The COVID-19 pandemic has significantly reduced the number of orthopedic surgeries worldwide. The main reason for this was an introduction of numerous restrictions in the field of mobility, which resulted in reduction of circumstances predisposing to injuries. This had a positive impact on the overall readiness of the health system to fight the pandemic, thanks to saving human and material resources that could be successfully allocated in order to fight a new, previously unknown threat. On the other hand, such aimed administration of the system was not indifferent in terms of care quality directed towards traumatized patients, often requiring immediate measures (risk of infection transmission). This study aims to evaluate in-hospital mortality in patients with COVID-19 operated on proximal femur fractures. An attempt was also made to determine predictors influencing mortality rate among patients operated over the analyzed period.

Keywords: COVID-19, proximal femur fracture, Polish experience with COVID-19, epidemiology, in-hospital mortality.

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Introduction

The first COVID-19 infections were reported in December 2019 in China. The conducted research indicated a number of common features of pneumonia, which were attributed to COVID-19 infection. These analyzes were multidirectional and included epidemiological, clinical and radiological data, but also on their basis, the first therapeutic schemes were proposed [1]. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to the coronavirus family of the β -coronavirus



2b line [2]. Some studies indicate its similarity to the known coronavirus transmitted by bats. Therefore, there was a suspicion that also in this case this mammal might have been a carrier [3]. On the other hand, other scientists express their uncertainty about illegally trafficked animals at a seafood fair in the city of Huanan [4]. COVID-19 has quickly turned into a global threat to the public health. Such situation obliged the World Health Organization (WHO) to take up immediate response, which resulted in the declaration of a global pandemic on February 11, 2020. The virus spread rapidly, causing serious problems to many health systems. In the following month, the first cases of SARS-CoV-2 infections were reported in Poland. This required the administrator of the health care system to undertake immediate decisions regarding introduction of appropriate activities aimed at counteracting the effects of the epidemic. The entire health care system had been divided into three levels, each of them assigned with a specific role to perform in this crisis situation (Table 1).

Table 1. Division of hospitals and their roles during the COVID-19 pandemic in Poland.

Level I hospitals	Level II hospitals	Level III hospitals
<ul style="list-style-type: none"> — increasing the number of beds allowing admission of a patient with suspected COVID-19 until the result of the examination is obtained or, if necessary, implementing life-saving procedures — organizational expansion of access to COVID-19 diagnostics by increasing the number of COVID-19 laboratories, developing standards that allow for more effective use of molecular and antigen tests 	<ul style="list-style-type: none"> — preparation of treatment rooms for patients with confirmed infection in each of the wards within their structure — creating safe zones for other patients to eliminate contact with those infected with COVID-19 	<ul style="list-style-type: none"> — otherwise known as coordinating hospitals based on the second level unit, where also non-infected patients can be treated

This structure evolved as the pandemic developed. Along with the increase in morbidity, also single-name hospitals (intended for treatment of infected patients only) and temporary hospitals were established either in the sports, commercial or premises of airport infrastructure etc. Our hospital was also transformed into a single-name hospital. In addition to structural changes, it was necessary to prepare a COVID-19 patient management scheme at every stage of specialized treatment. However, these recommendations continued to evolve with new information about the virus and its treatment. Maintaining certain standards was a big challenge for teams operating in restrictive sanitary regime. Each hospital ward had specific zones:

- red zone, intended for patients with confirmed or suspected coronavirus infection,
- orange zone where healthcare staff put on and took off personal protective equipment,
- green zone provided for all those without coronavirus confirmed.

During this period, our Trauma and Orthopedic Surgery Department focused primarily on treatment of patients requiring intervention because of various injuries of particular structures of the musculoskeletal system.

In the time of pandemic, any injuries in the elderly accompanied by comorbidities, are important for development of an appropriate treatment strategy. Proximal femur fracture is a life-threatening condition and any delay in surgery may adversely affect the clinical course through prolonged pain and immobilization of the patient. Therefore, in that (pandemic) situation, it also seemed most appropriate to act quickly and if possible, to upright the patient as early as possible, in order to shorten the period of lying down to necessary minimum. Such a procedure allows for greater pain control, minimizes blood loss, reduces mortality but also significantly reduces various complications (e.g. pneumonia and deep vein thrombosis). The patient achieves a relative faster improvement in the quality of life [5, 6]. Lv *et al.* report 4.9% of pulmonary complications as a result of surgical treatment of a femoral neck fracture [7]. Nevertheless, severe pneumonia may be a contraindication for the use of anesthetic and surgical procedures due to high risk of complications [8]. Orthopedic surgery should be avoided among infected people with severe dyspnoea (saturation <90%) and body temperature above 38 C having pneumonia and multiple organ system failure. Underlying diseases found among seniors such as diabetes, hypertension and heart disease are widely recognized as risk factors for increased mortality among infected patients [3, 9]. In that context obesity and chronic obstructive pulmonary disease should also be mentioned.

These difficult circumstances force orthopedic surgeons to make decisions, the consequences of which are difficult to predict. A life-saving operation needs to be performed however, there are doubts how to administer safety procedures on a person with acute respiratory failure. This situation somehow raises the question of the pathways of management in patients suffering from both bone fracture and COVID-19 infection. It is necessary to determine whether patients with a proximal femur fracture and infected with an acute respiratory distress virus have a higher risk of death from infection. The aim of our retrospective study was to analyze clinical data of patients operated on for proximal femur fracture and, in our opinion, to propose appropriate management methods. In addition, the goal was to establish the in-hospital mortality rate in COVID-19 infected patients operated on for a proximal femur fracture.

Methods and Material

The retrospective study covered the period from 01/02/2020 to 28/02/2022. It was the time when, depending on the severity of the pandemic, both patients infected with SARS-CoV-2 and those who were not infected were operated on in our Trauma and Orthopedic Surgery Department of the Independent Public Healthcare Center in Puławy. The study comprised only patients who had undergone surgical interventions due to proximal femur fracture. The research group consisted of 31 people with diagnosed COVID-19 infection (confirmed by an antigen test or PCR test). For comparison, in the discussed period (when our ward was opened to uninfected patients), the final analysis also included 87 patients without COVID-19 infection who required surgical treatment due to proximal femur fracture. The data obtained was following statistically analyzed. For quantitative features, a range of values (mix, max), standard deviation and medine were calculated.

Results

In the analyzed period, among the patients with proximal femur fracture, 31 patients were infected with the SARS-CoV-2. Additionally, chest computed tomography (CT) was performed in almost all patients. Twenty-four of them (77.4%) were women. The approximate age of the patients was 78.8 (SD = 9.3, median = 80, range 58–94) (Fig. 1). Twenty-four (77.4%) had intertrochanteric fracture, another two were diagnosed with subtrochanteric fracture, and five of the patients had femoral neck fracture (Fig. 2). All of them suffered after a fall at home (majority of them had no head injuries). In addition to a positive PCR or antigen test result, accompanying symptoms (fever, dyspnoea, desturation) were noted. Most had multiple comorbidities (Fig. 3), their mean number was 3.45 (SD = 2.54, median = 3, range = 0–8).

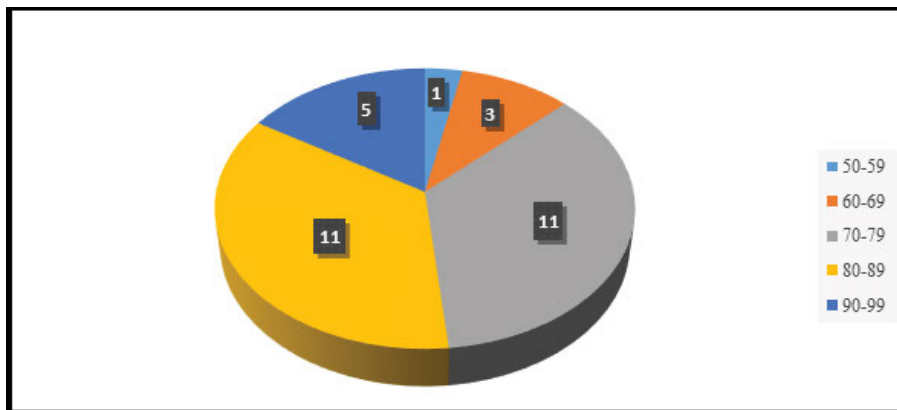


Fig. 1. Age of the study group.

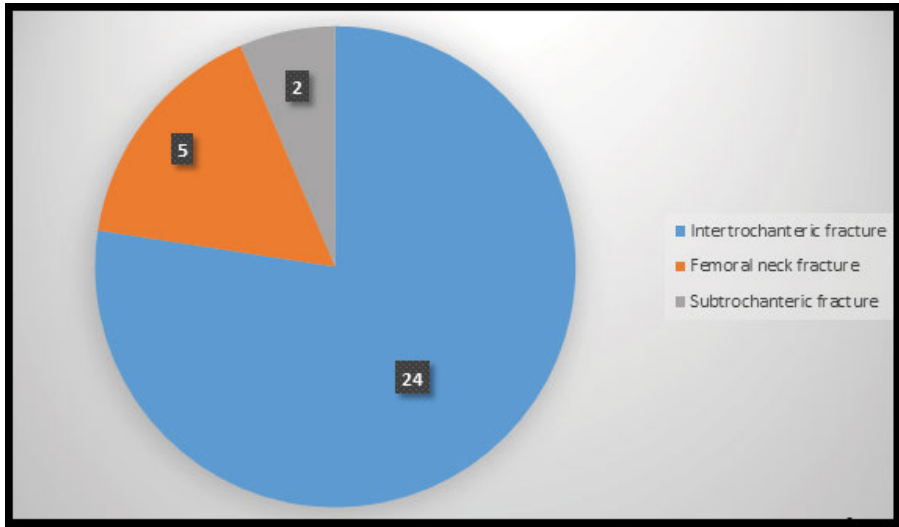


Fig. 2. Type of proximal femur fracture in COVID-19 patients.

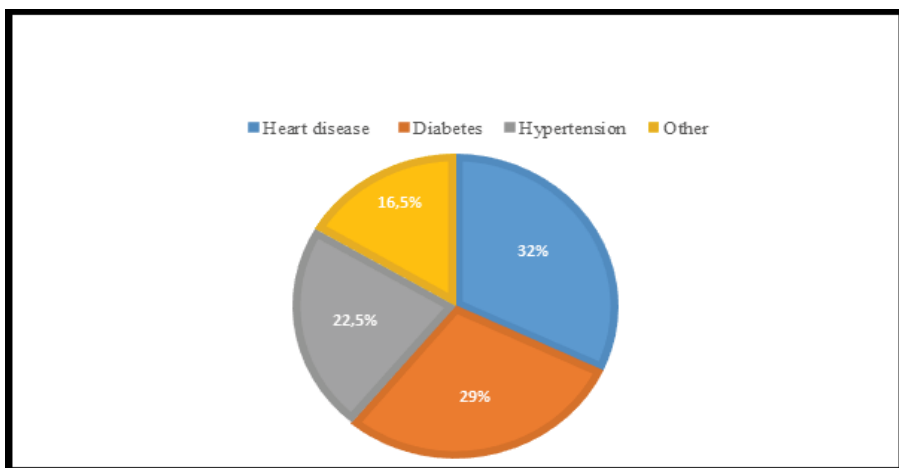


Fig. 3. Main comorbidities in patients with proximal femur fracture infected with COVID-19.

In addition, patients with interstitial pneumonia or related respiratory symptoms, according to the protocol, received pharmacotherapy, which included low molecular weight heparin (LMWH), standard hydration, steroids, antibiotic in case of suspected bacterial infection, and depending on the indications — Remdesivir, Tocilizumab, Baricitinib.

Eighteen people did not require oxygen therapy before the operation however, in sixteen cases it was necessary to administer oxygen afterwards in the same group. One

patient with no symptoms of interstitial pneumonia on CT and no need for oxygen therapy was immediately operated on the first day after hospitalization. The remaining patients, for various reasons, most often the need to stabilize their respiratory functions or withdraw after previously used anticoagulants, underwent surgical intervention in an average of 2–4 days after admission (74.2%).

Thirty-one patients were qualified for surgery according to anesthesiological recommendations and surgical conditions. One of the main criteria was peripheral oxygen saturation (pO_2) $>90\%$ and body temperature $<38^\circ\text{C}$. Most of the patients received spinal anesthesia. Patients with intertrochanteric and subtrochanteric fractures were fitted with intramedullary nail, while those with femoral neck fracture underwent bipolar hip prosthesis. In order to improve physiological ventilation, it was recommended in cases where it could be done on the first day after the surgery, to remain in a sitting position, to receive physiotherapists' assistance and, if possible, to put the patient upright as quickly as possible. Postoperative pain treatment was carried out on the basis of an analgesic ladder. In-hospital mortality was 22.5% (7 deaths), with the mean admission-to-death time which equalled 9.7 days (SD = 3.3 days, median = 10, range 6–16 days) (Fig. 4). Patients who successfully completed treatment (24 people) required an average of 15 days of hospitalization. That time was mainly due to generally accepted principles of isolating patients with COVID-19.

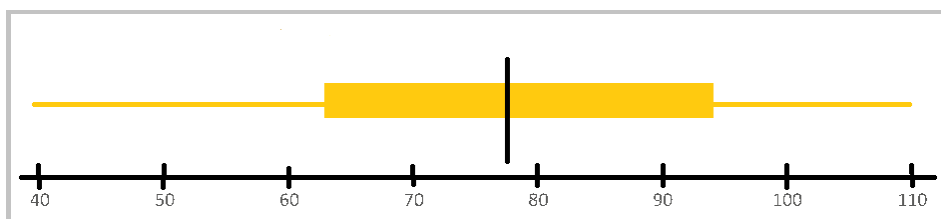


Fig. 4. Patients' mortality and age.

For example, in the same period, when the hospital was opened for patients not infected with COVID-19, 87 surgeries were performed at proximal femur (femoral neck fracture — 29 people, subtrochanteric fracture — 3 people and intertrochanteric fracture — 65 people) and out of the total 75.86% were women (Fig. 5). The average age of the patients was 80.66 (SD = 11, median = 84, range 52–101) (Fig. 6). There was one case of death on the second postoperative day. Statistically, the average waiting time for orthopedic intervention was 2.9 days, and the average postoperative stabilization time was 5.4 days. Most patients had co-existing symptoms and their mean amount was estimated at 1.5 (SD = 1.29, median = 2, range = 0–5). Average hospitalization time for patients undergoing this procedure was 7.98 days.

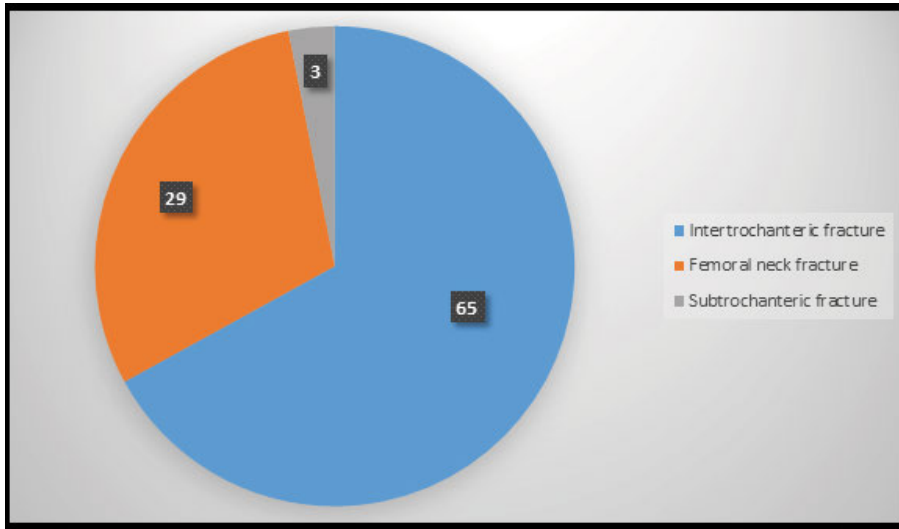


Fig. 5. Type of proximal femur fracture (uninfected patients).

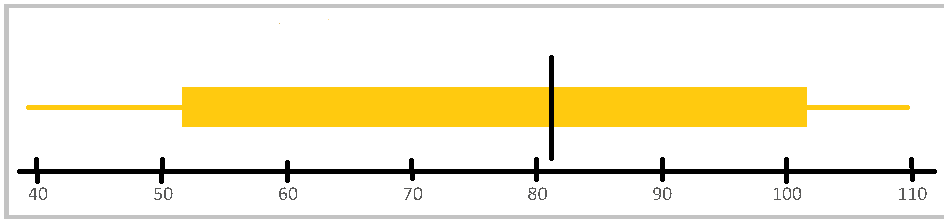


Fig. 6. Age of uninfected patients with proximal femur fracture.

Discussion

Hip fractures in elderly patients are most often accompanied by a high complication rate as well as high mortality rate [10]. Therefore, pre-pandemic recommendation was to perform surgery early enough, the standard care includes surgery within 48–72 hours after an injury. We mean here thromboembolic events, infections or bedsores. The above-mentioned complications directly extend hospitalization time, delay rehabilitation and thus contribute to higher mortality [11]. Pandemic development scale had a particularly negative impact on elderly population. Femoral neck fracture is normally associated with a significant percentage of deaths in these patients [12]. Despite the fact that there is an improvement in the ways of treatment, for example, in the United Kingdom in 2018 6.1% of patients died within 30 days after the injury [13]. The risk for the elderly increases significantly in the case of COVID-19 infection and the need for surgery due to femoral neck fracture. In general, the incidence of such

disease is estimated at 43–920 cases per 100,000 thousand population [14]. Pueyo-Sánchez *et al.* report the size of 620 cases per 100,000 people per year. Depending on the research, mortality is estimated at 20% to 40% in the first year and 7–8% within a month after the injury [15]. The pandemic period and all related limitations did not significantly reduce the scale of the phenomenon. There is a natural need to go shopping or use other public utility facilities (hospitals, pharmacies). Moving around at this age requires the use of general transport services. The above-mentioned factors enforce close contact situations, and thus increase the probability of an infection [16]. Such mobility may also constitute an opportunity for an injury. However, the main cause of any fractures lies in the mechanism of their formation. Most of the elderly people, despite pandemic social limitations, suffer injuries at home as a result of trips and falls from their own height [17]. In addition, most of them suffer from a number of comorbidities, which makes them extremely susceptible to pulmonary complications, especially those patients with lower limb fractures and the ones having forced limitation in mobility [18, 19]. The possibility of releasing pro-inflammatory cytokines increases with age, which may exacerbate the course of COVID-19 infection [20]. The need to undergo a surgery and hospital stay itself may also become a possibility of COVID-19 infection. Statistically, femoral neck fractures are quite common among the elderly. Moreover, such cases are not uncommon in the era of pandemic. This requires additional preparation of the team and operating theaters. It is suggested to implement adequate strategies during this difficult period. For example, Mi *et al.* recommend four main courses of action:

- in case of elderly people with minor fractures (e.g. distal radius fracture) in endemic areas, if possible, implement non-surgical treatment,
- fractures, in particular those scheduled for surgery, should be subject to strict infection control measures,
- a patient infected with COVID-19, who has pneumonia and additionally a bone fracture, is subject to intensive monitoring and treatment,
- surgery performed on a patient with bone fracture and pneumonia caused by COVID-19 should be led in a sub-pressure operating room [21].

Lower respiratory tract diseases in patients with proximal femur fractures are responsible for a significant percentage of complications. Another problem in this regard is the type of preoperative anesthesia. The risk of pulmonary disorders is larger with general anesthesia than with partial anesthesia, therefore, whenever possible, subarachnoid block should be used [22]. According to Ricci *et al.*, the period of hospitalization of uninfected patients undergoing the procedure of fracture fixation in the proximal femur (in this case, the femoral neck) depended on ASA classification, male gender and the need for additional cardiological examination [23]. The level of mortality associated with that procedure among people not infected with COVID-19 was also determined by the number of accompanying factors. Therefore, there are

significant discrepancies in medical publications assessing that issue. In our study, we obtained a result of less than one percent (0,78%), although others state higher values. For example, Sanz-Reig *et al.* (examined group of 331 people) 11.4%, Erikson *et al.* 1.5%, Lim *et al.* 2%. Walters *et al.* estimate 30-day mortality in a group of 326 people at 7.1% [24–27]. Munoz-Vives *et al.*, report mortality (14-day follow-up) in the group of 23 uninfected operated patients at 10.3% [28]. There are also much higher indices. Panula *et al.* indicate 27.3% mortality in the group of operated patients with a femoral neck fracture, which is three times higher than found among general population operated for other reasons at the same age [29]. The procedure performed within the first 48 hours after the fracture directly shortened the length of hospital stay and resulted in lower mortality and faster recovery [30]. In our group of uninfected operated patients (87), 45 people could have undergone the procedure at optimal time (48 hours after admission), which resulted in discharge in 10 of them in 3rd, 26 in 4th, and the rest of them in 5th–6th day after the surgery. This means that 47% of the patients required the surgery to be postponed for various reasons, which undoubtedly extended the total hospitalization time. This additionally influenced the implementation of appropriate pharmacological and other physiotherapy procedures.

Pre-surgery management of the infected patients with proximal femur fractures does not differ substantially from standard management for an uninfected patient, of course, with following sanitary regime appropriate for the infection. It is important to take steps to prevent deep vein thrombosis, pulmonary embolism and pressure ulcers. Based on our in-hospital observation of the group of 31 patients infected with COVID-19 operated for proximal femur fracture, we recorded seven deaths, which accounted for 22.5%. Due to the problems with blood oxygen saturation, it was not possible to perform the surgery in its optimal time. We achieved relative stabilization of the patient on day 2–5 after his admission to the Orthopedic and Traumatic Surgery Department. After surgery deaths resulted from progressive circulatory and respiratory failure caused by COVID-19. It happened on the 3rd–12th day following the operation. Catellani *et al.*, on the basis of their observation of ten COVID-19 infected patients with proximal femur fracture operated on the first day after admission report four postoperative deaths due to respiratory failure (one on the first day, two on the third day and one on the seventh day) [31]. Muñoz-Vives *et al.*, reported mean admission-to-surgery delay of 2.4 days (range 0–13) [28]. Many studies seem to confirm better results of an early surgery, also in infected patients. However, what is worth remembering and as confirmed by Cipollaro *et al.*, NSAIDs should be carefully administered in case of pro-inflammatory musculoskeletal pain among people with fractures and accompanying COVID-19 infection [32]. Tayyebi *et al.*, reported in-hospital mortality of 29.8% and mean hospital stay of 11.29 days [33]. In our study, the average hospitalization period of patients was 15 days. Lim *et al.* reported 13.2 days [26]. Mi *et al.*, analyzing a group of ten COVID-19 infected patients qualified for

proximal femur fracture surgery, recorded death of one patient 11 days after the operation, three others did not live to it. At the same time, they did not find an increased risk of postoperative complications [21]. Walters *et al.*, determined 30-day mortality at the level of 5.8%, while Kumar *et al.* estimated the mortality at 29.54% among patients undergoing proximal femur fracture fixation among the total number of them (orthopedic) in analyzed time [27, 34]. For example, Munoz-Vives *et al.* report mortality (14-day follow-up) in the group of operated patients infected with COVID-19 (23 people) at 30.4%. For comparison, among people treated conservatively (12), 8 of them died [28]. In turn, Mi *et al.* reported six cases of a proximal femur fracture, only three ultimately underwent surgery. Three in the examined group died (two as a result of conservative treatment, and one after the surgery) [21].

The authors suggest an attempt of conservative treatment in case of some fractures that do not require urgent surgical intervention. This view seems to be confirmed by Rabie *et al.*, who at the same time emphasize the importance of a flexible therapeutic approach to an infected patient. The patient's general condition, severity of the infection and level of risk when deciding on surgical intervention are becoming important in this regard. In such cases, the patient's condition is crucial. Aggravation of an infection symptoms and underlying diseases somehow force the surgery to be postponed [35]. In our case, most often (23 people, 74.2%) the patients were operated on day 2–4 following their admission.

Shariyate *et al.* argue that elderly patients with femoral neck fracture and with many comorbidities statistically more often have extended hospitalization time. In addition, their immune system is weakened due to their age, which results in faster multiplication of the virus which, in turn, affects significantly mortality rate [36]. Our observations show that with the average age of hospitalization (78.8 years), the patient's discharge most often took place between 9–13 days after admission, which accounted for 61.3% of the cases. In addition, nervous tension associated with the fracture and resulting surgery may cause the body's reaction to oxidative stress, causing inflammation, which may result in more severe course of infection, including an increased likelihood of pneumonia [36, 37]. This is especially significant in the case of COVID-19 infection, which we noticed in most of our elderly patients. Therefore, it is extremely important to pay special attention to the elderly, who are most susceptible to such situations. The COVIDSurg Collaborative study by Lancet analyzes all surgical cases with COVID-19 in 24 countries in terms of mortality within 7 and 30 days after the surgery, as well as pulmonary lesions. The 30-day mortality was 23.8% and the 7-day mortality 5.2%. Pulmonary complications were reported in 51.2% of cases, which automatically resulted in a higher death rate (38%), constituting 81.75% of the total number of deaths. Additionally, it was found that male gender together with the age over 70 dominate death statistics of the patients who underwent prior surgery [38]. In our study, the overall higher percentage of deaths among the operated patients

infected with COVID-19 was reported among women (71%), in addition 29% of deaths were the people under the age of 70. As the COVIDSurg Collaborative reports, an important factor that should be taken into account, are pulmonary complications noted among patients with perioperative infections. Out of a total of 1,128 cases, 299 were related to orthopedic intervention. There were 131 (44.3%) pulmonary complications, 86 people (28.8%) died. In the group of trauma patients (224) as many as 49.6% reported pulmonary complications, of which 67 cases ended in death. Therefore, in the time of the COVID-19 pandemic, a flexible approach to the surgical operations is suggested, especially in relation to patients over 70 years of age. If there is no such necessity, it should be considered to postpone surgery time or apply alternative (non-surgical) treatment. In the COVIDSurg study, the American Society of Anaesthesiology (ASA) classification was used to predict the scale of 30-day pulmonary complications and 7-day mortality. Grade 3–5 was considered to be the most predisposing of patients to both pulmonary complications and death within seven days after the surgery [38]. In conclusion, non-urgent surgical procedures may be postponed and non-surgical treatment should be promoted to delay or avoid the need for surgery. Strategies to reduce SARS-CoV-2 transmission and the risk of postoperative complications should be planned. Due to the fact that orthopedic surgeries are by their nature very invasive and usually require prolonged anesthesia, it is recommended to perform only those that are absolutely necessary.

An advantage of the study is that it features a different type of fracture of the proximal femur. Most of the analyzes concern femoral neck fractures, which in our study accounted for a negligible percentage of the total number of cases. Much more these were intertrochanteric fractures which we recorded. A small research group seems to be a limitation, which may affect the final results.

Conclusions

COVID-19 pandemic has led to a significant reduction in the number of fracture patients worldwide, although occurrence of osteoporotic fractures (including proximal femur fractures) remains the same. There should be recommended a conservative management of fractures that do not require immediate surgical intervention. Any others, including proximal femur fractures, displaced fractures, severe limb injuries and open fractures require immediate action. All postoperative complications are the result of pro-inflammatory cytokines and immunosuppressive responses to surgical intervention and mechanical ventilation. Additionally, people with COVID-19 infection are particularly susceptible to thromboembolic events. Therefore, unless there are contraindications, it is necessary to supplement at least standard doses of heparin. Another option in high-risk patients is to use mechanical anticoagulant prophylaxis.

The discussed proximal femur fracture itself is associated with a higher risk of perioperative mortality, while the fracture in the above-mentioned location together with the accompanying COVID-19 infection increases risk itself even more, which is confirmed by our research.

In addition, the importance of comorbidities that significantly affect mortality rate but also reduce the pace of postoperative recovery in patients infected with COVID-19, should be particularly emphasized. All the diseases that somehow impair functioning of the respiratory system seem to be as important. Advanced age negatively affects mortality rates, however, from our point of view, a set of previously acquired factors is of great importance, as their dynamics exacerbate the course of postoperative COVID-19 infection. Nevertheless, each operation in the time of pandemic period should be preceded by a thorough analysis and observance of strict precautionary measures.

Conflict of interest

None declared.

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