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Research Article

Predictive factors associated with thirty-day mortality in geriatric patients with hip fractures

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ABSTRACT

Objective: This study aimed to determine the predictive factors affecting the 30-day mortality in geriatric hip fractures, investigate the effect of the timing of surgery, and thus determine the optimum cut-off time in delaying the surgery.

Methods: A total of 596 patients(205 men, 391 women; mean age = 78.3 years) were included in this retrospective study. All possible predictive factors encountered in the literature review, including age, sex, fracture type, comorbidities, American Society of Anesthesiologists (ASA) score, surgical delay time, anaesthesia type, surgery type, need for erythrocyte replacement, postoperative complications, and the need for postoperative intensive care were analyzed. The predictive factors that were found to be significant as a result of the univariate analysis were included in the multivariate logistic regression analysis.

Results: The reason for surgery was an extracapsular fracture in 359 patients (60.2%) and an intracapsular fracture in 237 (39.8%). Arthroplasty was performed in 256 patients (43%), while proximal femoral nails were used in 251 (42.1%), dynamic hips screws in 68 (11.4%), and cannulated screws in 21 (3.5%). 523 (87.8%) of the patients had an ASA score of 1 or 2, and 73 (12.2%) had an ASA score of 3 or 4. General anaesthesia was performed on 35.2% of the patients, while regional anaesthesia was administered to 64.8%. Major complications developed in 42 patients (7%), while minor complications were observed in 143 (24%). The mean surgical delay time was 3.21 days (1-9 days). The ASA score ($P < 0.001$, OR: 56.83, CI: 5.26-2.820), anesthesia type ($P = 0.036$, OR: 3.225, CI: 0.079-2.264), surgical delay time ($P < 0.001$, OR: 2.006, CI: 1.02-0.372) and major complication ($P = 0.002$, OR: 6.41, CI: 0.661-3.053) were determined to be predictive factors of 30-day mortality.

Conclusion: This study found the median surgical delay time as three days in surviving patients and five days in deceased ones. Thus, a 3-day surgical delay may be acceptable and sufficient for medical optimization and the consensus of the multidisciplinary team.

Level of Evidence: Level IV, Therapeutic Study

Introduction

The incidence of geriatric hip fractures is increasing globally and becoming a major public health problem. Of the 9 million osteoporotic fractures that occurred worldwide in 2000, 1.6 million were hip fractures.[1] Even if the incidence of hip fractures remains unchanged, this number is expected to reach 6.26 million by 2050.[2] Ninety-five percent of adult hip fractures are treated surgically.[3] It is a known fact that the mortality and major complication rates in the early and late terms are high after geriatric hip fractures.[4] Studies examining the effects of fracture localization (intracapsular/extracapsular), age and comorbidities of the patient, timing of surgery, anesthesia type (regional/general), and surgery type (internal fixation/arthroplasty) on mortality have reported different results.[5-7] The treatment method for geriatric hip fractures requires a multidisciplinary approach due to the high comorbidity rate, and thus different interdisciplinary approaches can be seen in clinical practice. The advantages and disadvantages of medical optimization and expedited surgery are still controversial. While some studies suggested that delaying the surgery increases mortality, there are also studies asserting the opposite.[8-31] In addition, different opinions exist regarding the cut-off time for surgical delay. Our main aim in this study was to determine the predictive factors affecting the 30-day mortality after geriatric hip fractures. We also aimed to investigate the effect of the timing of surgery on mortality and thus determine the best cut-off time in surgical delay. In addition, by examining the reasons for surgical delay, we tried to obtain evidence for interdisciplinary harmony.

Materials and Methods

A total of 743 patients with a hip fracture that were surgically treated in our clinic between January 2011 and June 2021 were retrospectively reviewed. After excluding the patients who were under the age of 60 and were admitted to the hospital 12 hours after trauma, and those who had a history of high-energy trauma or second surgery due to any reason within 30 days after the first surgery, had pathological fractures, or had insufficient or inconsistent preoperative data, 596 patients (205 men, 391 women; mean age: 78.3 [range: 60 to 102] years) were included in this retrospective comparative study. Patient selection flowchart is given in Figure 1. The computerized data, hospital charts, and radiological images of these patients were examined. Patients with conflicting data were also excluded from the study. Other data including age at admission, sex, fracture type (intracapsular/extracapsular), comorbidities,

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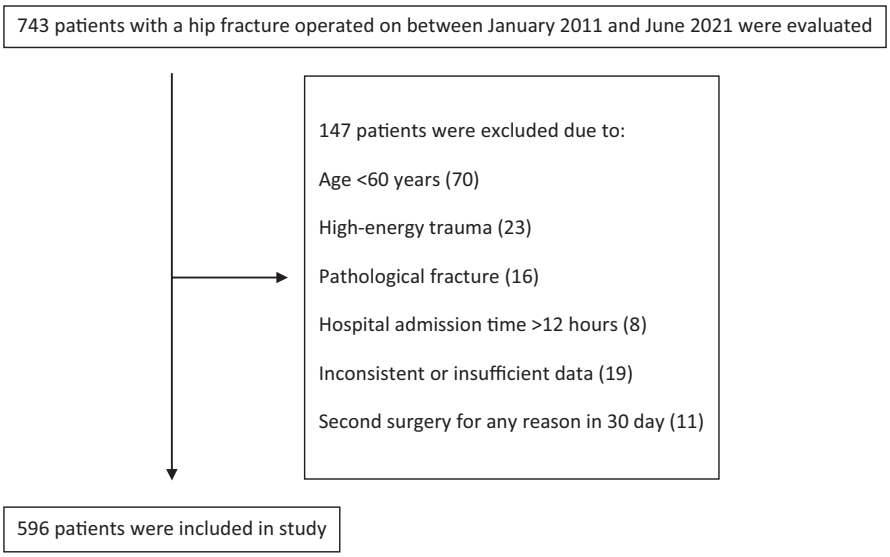

Figure 1. Flowchart demonstrating the exclusion criteria.

American Society of Anesthesiologists (ASA) score, admission date, surgery date, anesthesia type (regional/general), surgery type (internal fixation/arthroplasty), use of antiaggregants or anticoagulants, need for erythrocyte replacement, complications, and the need for postoperative intensive care were also analyzed.

In accordance with the literature, the patients were divided into 2 groups; those aged 75 years or over and those below 75.[32] Preoperative radiological images of the patients were examined and femoral neck fractures were grouped as intracapsular fractures and trochanteric fractures as extracapsular fractures. Detailed preoperative data such as comorbidities and ASA score were retrieved from the anesthesiology evaluation charts, consultation charts, and computerized data of the patients. Comorbidities were classified into 6 groups: cardiac system, pulmonary system, renal system, central nervous system, endocrine system, and gastrointestinal system. The classification of the comorbidities was made in reference to similar studies in the literature and based on our clinical experience.[7,12] The ASA scores were grouped as 1-2 or 3-4, again in accordance with previous studies.[33] The surgical delay time in days was calculated as the difference between presentation and surgery dates and was analyzed as continuous data. The surgery type was determined after examining the postoperative radiological images of the patients and classified as proximal femoral nail (PFN), dynamic hip screw (DHS), or cannulated screw application based on the method preferred for internal fixation.

Since the reason for delaying the surgery was usually the use of antiaggregants and anticoagulants, the data on the use of warfarin, low-molecular-weight heparin (LMWH), clopidogrel, acetyl salicylic acid, rivaroxaban, and dabigatran were analyzed. Postoperative complications were classified as life-threatening and major complications (mortality, pulmonary embolism, cardiac arrest, myocardial infarction, unplanned intubation, sepsis, acute renal failure, and cerebrovascular accident) or non-life-threatening and minor complications (urinary tract infection, deep vein thrombosis, pneumonia, peripheral nerve injury, and superficial wound infection). The 30-day mortality rate was determined by using the national data system and by telephone interviews. Permission was obtained from the local ethics commission prior to the study (June 15, 2021/25). Since this study was a retrospective study, written informed consent was not obtained.

HIGHLIGHTS

- Geriatric hip fractures are a major public health problem. The optimal time for surgery is still a matter of debate. This study aimed to determine the predictive factors affecting the 30-day mortality after geriatric hip fractures and investigate the timing of surgery on mortality.
- The results showed that the ASA score, renal and central nervous system comorbidities, anesthesia type, delayed surgery and incidence of major complication were predictive factors for 30-day mortality.
- The results from this study indicate that surgery should be performed within three days after admission. A multidisciplinary team approach may decrease time to surgery and thus decrease mortality.

Statistical analyses

The continuous data are given as average ± standard deviation and the categorical data are given as percent. The Shapiro–Wilk test was used to investigate the normality of data. The Mann–Whitney *U* test was used to compare 2 groups that did not exhibit normal distribution, while in the analysis of crosstab tables, Pearson's chi-square and exact tests were utilized. The risk factors were determined using multivariate logistics regression analysis. The International Business Machines Statistical Package or the Social Sciences for Windows v.21.0 software (IBM Corp., Armonk, NY, USA) was used for the statistical analyses. The level of significance was set at $P < 0.05$.

Results

The reason for surgery was an extracapsular fracture in 359 patients (60.2%) and an intracapsular fracture in 237 (39.8%). Arthroplasty was performed in 256 patients (43%), while PFNs were used in 251 (42.1%), DHSs in 68 (11.4%) patients, and cannulated screws in 21 (3.5%). While 523 patients (87.8%) had an ASA score of 1 or 2, 73 (12.2%) had an ASA score of 3 or 4. Regarding comorbidities, 69.8% of the patients had cardiac system, 24.3% pulmonary system, 16.3% renal system, 27.5% central nervous system, 31.5% endocrine system, and 3.7% gastrointestinal system diseases. General anesthesia was administered to 35.2% of the patients, while regional anesthesia was administered to 64.8%. Erythrocyte replacement was performed in 39.9% of the patients. Major complications developed in 42 patients (7%), while minor complications were observed in 143 (24%). In 46 patients (7.7%), the need for postoperative intensive care developed. The mean surgical delay time was 3.21 days (range: 1-9 days). The baseline characteristics of the patients are summarized in Table 1.

Table 1. Baseline characteristics of the study population

Characteristics		Count	Percentage
Sex	Men	205	34.4
	Women	391	65.6
Age, years	60-74	188	31.5
	≥75	408	68.5
Surgery type	Arthroplasty	256	42.3
	PFN	251	42.1
	DHS	68	11.4
	Cannulated screw	21	3.5
Fracture type	Extracapsular	359	60.2
	Intracapsular	237	39.8
ASA score	1-2	523	87.8
	3-4	73	12.2
Comorbidities	Cardiac	416	69.8
	Pulmonary	145	24.3
	Renal	97	16.3
	Central nervous	164	27.5
	Endocrine	188	31.5
	Gastrointestinal	22	3.7
Antiaggregant or anticoagulant use	Acetyl salicylic acid	107	18
	Clopidogrel	52	8.7
	Warfarin	26	4.4
	LMWH	2	0.3
	Rivaroxaban	7	1.2
	Dabigatran	4	0.7
	None	398	66.8
Anesthesia type	General	210	35.2
	Regional	386	64.8
Erythrocyte replacement	Yes	238	39.9
	No	358	60.1
Major complication	Yes	42	7
	No	554	93
Minor complication	Yes	143	24
	No	453	76
Intensive care requirement	Yes	48	8.1
	No	548	91.9
30-day mortality	Died	38	6.4
	Survived	558	93.6

DHS, dynamic hip screw; LMWH, low-molecular-weight heparin; PFN, proximal femoral nail; ASA, American Society of Anesthesiologists.

30-day mortality

The 30-day mortality rate was 6.5% (38 patients). It was observed that the causes of death of the patients were pulmonary embolism, congestive heart failure, pulmonary infection, myocardial infarction, septic shock, and stroke. In some patients, the cause of death could not be determined due to death at home. Detailed causes of death are given in Table 2. Of the patients who died, 14 (36.8%) were men and 24 (63.2%) were women. The high mortality rate in women was not statistically significant ($P=0.681$). The mean age of the 38 patients who died was 80.63 years, while the mean age of the 558 patients who survived was 78.21 years. Age was not found to be a statistically significant factor for the 30-day mortality ($P=0.075$). Of the 38 patients who died, 18 underwent arthroplasty, 1 underwent DHS, and 19 underwent PFN surgeries. No significant relationship was found between surgery type and mortality ($P=0.279$). Twenty-one (5.8%) of the 359 patients with extracapsular fractures and 17 (7.2%) of the 237 patients with intracapsular fractures died. No significant relationship was found between fracture type and mortality ($P=0.517$).

Of the 38 patients who died, 33 had an ASA score of 3 or 4, while only 5 had an ASA score of 1 or 2. In other words, 33 (45.2%) of the 73 patients with an ASA score of 3 or 4 died. A significant relationship was found between ASA score and mortality ($P<0.001$). Regarding comorbidities, there was a significant relationship between mortality and renal system and central nervous system diseases ($P=0.025$ and $P=0.011$), while no significant relationship was observed between mortality and cardiac system, pulmonary system, endocrine system, and gastrointestinal system diseases ($P=0.204$, $P=0.065$, $P=0.735$ and $P=0.139$, respectively). While 20 of the 38 patients who died did not use any anticoagulants or antiaggregants, 9 of them used acetylsalicylic acid, 6 used clopidogrel, and 3 used warfarin. No significant relationship was observed between antiaggregant/anticoagulant use and mortality ($P=0.35$). Twenty-one (10%) of the 210 patients who had received general anesthesia and 17 (4.4%) of the 386 patients who had received regional anesthesia died. The difference was statistically significant ($P=0.006$).

Table 2. Distribution of patients with 30-day mortality according to causes of death

Reasons of death	30-day mortality
Pulmonary embolism	**6**
Congestive heart failure	**7**
Pulmonary infection	**7**
Myocardial infarction	**2**
Septic shock	**5**
Stroke	**1**
Unknown*	**10**
Total	**38**

*Patients whose cause of death cannot be determined due to death at home.

While the mean surgical delay time was 4.85 (standard deviation (SD): 1.47) days in the 38 patients who died, it was 3.08 (SD: 1.66) days in the 548 patients who survived. The difference was again statistically significant ($P<0.001$). 8.5% of the patients who underwent erythrocyte replacement and 5.1% of the patients who did not undergo erythrocyte replacement died. The difference in this analysis was not enough to conclude a significant relationship between erythrocyte replacement and mortality ($P=0.098$). Of the 143 patients with minor complications, 5 (3.5%) died, suggesting no significant relationship with mortality ($P=0.109$). Of the 48 patients with a history of intensive care, 19 (39.6%) died, suggesting a significant relationship with mortality ($P<0.001$). Major complications were observed in 23 (60.5%) of the 38 patients who died, pointing out to a significant relationship with mortality ($P<0.001$). The univariate analysis of the predictive factors affecting the 30-day mortality is shown in Table 3.

The ASA score, surgical delay time, anesthesia type, renal and central nervous system comorbidities, intensive care history, and major complication factors, which were determined to be significant predictors of mortality as a result of the univariate analysis, were evaluated with multivariate logistic regression analysis. As a result of this analysis, the ASA score ($P<0.001$, OR: 56.83, CI: 5.26-2.820), anesthesia type ($P=0.036$, OR: 3.225, CI: 0.079-2.264), surgical delay time ($P<0.001$, OR: 2.006, CI: 1.02-0.372), and major complication ($P=0.002$, OR: 6.41, CI: 0.661-3.053) were determined to be predictive factors of the 30-day mortality. Results of the multivariate analysis are summarized in Table 3.

Discussion

In this study, we retrospectively analyzed 596 hip fracture patients to determine 30-day mortality and predictive factors in geriatric proximal femur fractures. Although our sample size was not very large, the range of relevant confounders was wide. In addition, excluding patients aged <60 years and patients with fractures as a result of a

Table 3. Univariate regression and multivariate logistic regression analyses results

		30-day mortality			
		Univariate regression	Multivariate regression		
Predictive factors		***P***	**OR**	**CI**	***P***
Sex		0.681			
Age		0.075			
Surgery type		0.279			
Fracture type		0.517			
ASA score (3-4)		**<0.001**	56.830	5.260-2.820	**<0.001**
Comorbidities	*Cardiac*	0.204			
	Pulmonary	0.065			
	Renal	**0.025**			
	Central nervous	**0.011**			
	Endocrine	0.735			
	Gastrointestinal	0.139			
Antiaggregant or anticoagulant use		0.350			
Anesthesia type (general)		**0.006**	3.225	0.079-2.264	**0.036**
Erythrocyte replacement		0.098			
Major complication		**<0.001**	6.410	0.661-3.053	**0.002**
Minor complication		0.109			
Intensive care requirement		**<0.001**			
Surgery delay		**<0.001**	2.006	1.020-0.372	

ASA, American Society of Anesthesiologists; OR, odds ratio. Statistically significant *P* values are given in bold.

high-energy trauma, while including fragility fractures in the study made our study more practical. A more reliable regression analysis was aimed by not classifying the surgical delay time and evaluating the confounders as continuously as possible. By those means, we aimed to determine a cut-off value for surgical delay that affects mortality. In addition, the 30-day mortality, which is easier to interpret and less likely to be affected by other factors, was examined in our study.

In the present study, the 30-day mortality rate was 6.4%, which is consistent with the results from the literature.[27] Our study showed that gender was not a significant predictive factor for mortality. This study showed that gender was not a significant predictive factor for mortality. The literature holds some studies showing that male gender increases mortality[9,11,14-16,33,34] and some others reporting otherwise,[6,7,17] rendering this relationship a controversial one. Contrary to a large number of studies in the literature,[7,9,11,13,17,18,32-34] our study showed that age was not a significant predictive factor for mortality. This was due to the age distribution in our patient group. In our opinion, the fact that 68.5% of our patients were 75 years or older and that the varying distributions of the patients in terms of age, ASA score, and surgical delay time may have caused this situation. This may be due to the fact that 68.5% of our patients were aged 75 years and above, and the distribution of the patients in terms of age, ASA score, and surgical delay time.

This study supports the argument that ASA score is a strong predictive factor of the 30-day mortality ($P < 0.001$) Since the ASA score's strong effect on mortality, easy interpretation, and widespread acceptance have been shown in many studies,[7,9,11,13,33,34] it is a reliable and useful predictive factor. In numerous survival studies, a higher mortality rate was reported in trochanteric fractures than in neck fractures.[5,13,19,20,21] However, there was no correlation between fracture type and mortality in this study. Similar to this results, some studies also have not found a relationship between fracture type and mortality.[6,7,17] The relationship between fracture type and mortality is controversial considering that patients with trochanteric fractures have higher comorbidities and are older, although some multivariate analyses have supported this relationship. This study stated that there was no significant relationship between the type of surgery and mortality. Different than similar studies, we separately evaluated the types of internal fixation. While there are studies reporting similar results to this study,[6,17] some others reported high mortality in patients who underwent arthroplasty.[24,32] In this study, anesthesia type was associated with mortality ($P = 0.036$). This result is compatible with others from studies reporting that regional anesthesia reduces mortality.[22,23]

In this study, the surgical delay time was very long. When we examined the reasons for this situation, we encountered factors such as prolonged preoperative evaluation period, use of antiaggregants and anticoagulants, unfitting surgical team, and inadequate intensive care conditions. The most important factor we frequently encountered was delaying the surgery for preoperative evaluation and medical optimization. In the literature, discussions on the balance between medical optimization and early surgery continue, with the challenges of different interdisciplinary approaches in parallel. This situation emerges as the most important reason for the prolongation of the surgical delay time. This study stated that delaying the surgery was associated with 30-day mortality ($P < 0.001$). Unlike many studies in the literature,[11-13,32] we analyzed the surgery delay period as a continuous value by not classifying it. In this way, it was aimed to strengthen the regression analysis and find a cut-off value. This study mentioned that the median surgical delay time was 3 days in surviving patients and 5 days in deceased ones. Therefore, 3-day delay is acceptable and this period may be sufficient for medical optimization. Bretherton and Parker[13] reported that surgery within the first 12 hours reduced the 30-day mortality and that surgery performed within the next 48 hours did not cause a significant decrease in mortality. Uzoigwe et al[25] and Nyholm et al[9] also reported that surgery performed within the first 12 hours reduced mortality. Carretta et al[11] reported that surgery performed within the first 48 hours reduced the 30-day mortality. A meta-analysis by Simunovic et al[10] supports the assertion of low mortality in patients who underwent early surgery. According to Shiga et al[30] showed that surgery after 48 hours increased mortality. While there are many studies showing the effect of delaying surgery on mortality, there are others reporting the opposite.[30,35-37] Öztürk et al[36] found a relationship between surgical delay and 30-day mortality in hip fracture surgery patients with no or moderate comorbidity, whereas they failed to put forward the same relationship in hip fracture patients with a high comorbidity level.

The largest prospective randomized controlled trial on this matter showed that accelerated surgery did not reduce the 90-day mortality or major complications compared to standard care in patients with hip fractures. However, accelerated surgery has been reported to be associated with a lower risk of delirium, faster mobilization, and shorter hospital stay.[8] However, in this study, patients aged 45 years and older were examined and the accelerated group was operated on within the first 6 hours on average, and the standard group within the first 24 hours on average. It has been suggested by various organizations that the acceptable limit for surgical delay is 24 hours,[27] 48 hours,[28] and most recently 36 hours as recommended by NICE.[29] In this study, 36 hours stands out as an acceptable delay time, in line with NICE's recommendation.[29] However, these figures lack conclusive evidence. A recent meta-analysis has loosely recommended early surgery to be beneficial but acknowledged that the lack

of prospective studies and inadequate adjustment for confounding factors hindered definitive conclusions, particularly when it comes to the 30-day mortality.[30] Multivariate analysis was performed by analyzing all possible confounders.

Although we tried to strengthen our study by removing 19 patients with incomplete and contradictory data, we accept that this was a limitation. The fact that our study might not reflect the general trend since it is a single-center study was another limitation. The relatively small size of our sample group and the retrospective nature of the study were other limitations. On the other hand, we strengthened our study by analyzing almost all potential confounders examined in the literature. In addition, by analyzing the surgical delay time as a continuous variable, we were able to determine a cut-off time, which was one of the main aims of our study. With this study, we aimed to contribute to the determination of an acceptable delay time, which has been extensively researched in the literature.

In conclusion, of the factors affecting mortality in geriatric hip fractures, only surgical delay time can be modified. It is widely accepted that delaying the surgery increases mortality. All studies have shown the negative effect of delaying surgery on other complications and length of hospital stay. It is possible to shorten the surgical time with the consensus of a multidisciplinary team involved in the management of geriatric hip fractures on a common concept. In addition, with the support of hospital administrators and trauma coordinators, a more effective treatment opportunity will be possible by assigning a separate operation room and team for this patient group.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Eskişehir Osmangazi University (Approval No: June 15, 2021/25).

Informed Consent: N/A.

Author Contributions: Concept - M.K., U.İ.; Design - M.K., S.O.; Supervision - M.K., U.İ.; Materials - M.K., S.O.; Data Collection and/or Processing - S.O., Z.A.; Analysis and/or Interpretation - S.O., Z.A.; Literature Review - S.O., Z.A.; Writing - M.K., S.O.; Critical Review - U.İ.

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References

1. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. *Osteoporos Int*. 2006;17(12):1726-1733. [CrossRef]
2. Cooper C, Campion G, Melton LJ 3rd. Hip fractures in the elderly: a world-wide projection. *Osteoporos Int*. 1992;2(6):285-289. [CrossRef]
3. Royal College of Physicians. *National Hip Fracture Database Annual Report 2018*. London: Royal College of Physicians; 2018.
4. Farahmand BY, Michaëlsson K, Ahlbom A, Ljunghall S, Baron JA, Swedish Hip Fracture Study Group. Survival after hip fracture. *Osteoporos Int*. 2005;16(12):1583-1590. [CrossRef]
5. Fox KM, Magaziner J, Hebel JR, Kenzora JE, Kashner TM. Intertrochanteric versus femoral neck hip fractures: differential characteristics, treatment, and sequelae. *J Gerontol A Biol Sci Med Sci*. 1999;54(12):M635-M640. [CrossRef]
6. Kenzora JE, McCarthy RE, Lowell JD, Sledge CB. Hip fracture mortality. Relation to age, treatment, preoperative illness, time of surgery, and complications. *Clin Orthop Relat Res*. 1984;186(186):45-56.
7. Kesmezacar H, Ayhan E, Unlu MC, Seker A, Karaca S. Predictors of mortality in elderly patients with an intertrochanteric or a femoral neck fracture. *J Trauma*. 2010;68(1):153-158. [CrossRef]
8. HIP ATTACK Investigators. Accelerated surgery versus standard care in hip fracture (HIP ATTACK): an international, randomised, controlled trial. *Lancet*. 2020;395(10225):698-708. [CrossRef]
9. Nyholm AM, Gromov K, Palm H, et al. Time to surgery is associated with thirty-day and ninety-day mortality after proximal femoral fracture: a retrospective observational study on prospectively collected data from the Danish fracture database collaborators. *J Bone Joint Surg Am*. 2015;97(16):1333-1339. [CrossRef]
10. Simunovic N, Devereaux PJ, Sprague S, et al. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. *CMAJ*. 2010;182(15):1609-1616. [CrossRef]
11. Carretta E, Bochicchio V, Rucci P, Fabbri G, Laus M, Fantini MP. Hip fracture: effectiveness of early surgery to prevent 30-day mortality. *Int Orthop*. 2011;35(3):419-424. [CrossRef]
12. Sexson SB, Lehner JT. Factors affecting hip fracture mortality. *J Orthop Trauma*. 1987;1(4):298-305. [CrossRef]
13. Bretherton CP, Parker MJ. Early surgery for patients with a fracture of the hip decreases 30-day mortality. *Bone Joint J*. 2015;97-B(1):104-108. [CrossRef]
14. White BL, Fisher WD, Laurin CA. Rate of mortality for elderly patients after fracture of the hip in the 1980's. *J Bone Joint Surg Am*. 1987;69(9):1335-1340. [CrossRef]
15. Clayer MT, Bauze RJ. Morbidity and mortality following fractures of the femoral neck and trochanteric region: analysis of risk factors. *J Trauma*. 1989;29(12):1673-1678. [CrossRef]
16. Magaziner J, Simonsick EM, Kashner TM, Hebel JR, Kenzora JE. Survival experience of aged hip fracture patients. *Am J Public Health*. 1989;79(3):274-278. [CrossRef]
17. Aharonoff GB, Koval KJ, Skovron ML, Zuckerman JD. Hip fractures in the elderly: predictors of one year mortality. *J Orthop Trauma*. 1997;11(3):162-165. [CrossRef]
18. Schrøder HM, Erlandsen M. Age and sex as determinants of mortality after hip fracture: 3,895 patients followed for 2.5-18.5 years. *J Orthop Trauma*. 1993;7(6):525-531. [CrossRef]
19. Haentjens P, Autier P, Barette M, et al. Survival and functional outcome according to hip fracture type: a one-year prospective cohort study in elderly women with an intertrochanteric or femoral neck fracture. *Bone*. 2007;41(6):958-964. [CrossRef]
20. Keene GS, Parker MJ, Pryor GA. Mortality and morbidity after hip fractures. *BMJ*. 1993;307(6914):1248-1250. [CrossRef]
21. Beaupre LA, Jones CA, Saunders LD, Johnston DW, Buckingham J, Majumdar SR. Best practices for elderly hip fracture patients. A systematic overview of the evidence. *J Gen Intern Med*. 2005;20(11):1019-1025. [CrossRef]
22. Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. *BMJ*. 2000;321(7275):1493. [CrossRef]
23. Karagiannis A, Papakitsou E, Dretakis K, et al. Mortality rates of patients with a hip fracture in a southwestern district of Greece: ten-year follow-up with reference to the type of fracture. *Calcif Tissue Int*. 2006;78(2):72-77. [CrossRef]
24. Vestergaard P, Rejnmark L, Mosekilde L. Has mortality after a hip fracture increased? *J Am Geriatr Soc*. 2007;55(11):1720-1726. [CrossRef]
25. Uzoigwe CE, Burnand HG, Cheesman CL, Aghedo DO, Faizi M, Middleton RG. Early and ultra-early surgery in hip fracture patients improves survival. *Injury*. 2013;44(6):726-729. [CrossRef]
26. No authors listed. *National Hip Fracture Database: National Report*; 2013. Available at: http://www.nhfd.co.uk/20/hipfractureR.nsf/vwcontent/2013ReportDownload/$File/onlineNHFDreport.pdf?openelement; (date of access: 24 September 2014).
27. No authors listed. Fractured neck of femur. Prevention and management. Summary and recommendations of a report of the Royal College of Physicians. *J R Coll Phys Lond*. 1989;23(1):8-12.
28. No authors listed. British Orthopaedic Association: the care of patients with fragility fracture; 2007. Available at: https://www.bgs.org.uk/sites/default/files/content/attachment/2018-05-02/Blue%20Book%20on%20fragility%20fracture%20care.pdf; (date of access: 24 September 2014).
29. No authors listed. *Hip Fracture: the Management of Hip Fracture in Adults* [NICE guidelines]; 2011. Available at: http://www.nice.org.uk/guidance/CG124; (date of access: 24 September 2014).
30. Shiga T, Wajima Z, Ohe Y. Is operative delay associated with increased mortality of hip fracture patients? Systematic review, meta-analysis, and meta-regression. *Can J Anaesth*. 2008;55(3):146-154. [CrossRef]
31. Khan SK, Kalra S, Khanna A, Thiruvengada MM, Parker MJ. Timing of surgery for hip fractures: a systematic review of 52 published studies involving 291,413 patients. *Injury*. 2009;40(7):692-697. [CrossRef]
32. Rosso F, Dettoni F, Bonasia DE, et al. Prognostic factors for mortality after hip fracture: operation within 48 hours is mandatory. *Injury*. 2016;47(suppl 4):S91-S97. [CrossRef]
33. Carow J, Carow JB, Coburn M, et al. Mortality and cardiorespiratory complications in trochanteric femoral fractures: a ten year retrospective analysis. *Int Orthop*. 2017;41(11):2371-2380. [CrossRef]
34. Kempenaers K, Van Calster B, Vandoren C, et al. Are the current guidelines for surgical delay in hip fractures too rigid? A single center assessment of mortality and economics. *Injury*. 2018;49(6):1169-1175. [CrossRef]
35. Grimes JP, Gregory PM, Noveck H, Butler MS, Carson JL. The effects of time-to-surgery on mortality and morbidity in patients following hip fracture. *Am J Med*. 2002;112(9):702-709. [CrossRef]
36. Öztürk B, Johnsen SP, Röck ND, Pedersen L, Pedersen AB. Impact of comorbidity on the association between surgery delay and mortality in hip fracture patients: a Danish nationwide cohort study. *Injury*. 2019;50(2):424-431. [CrossRef]
37. Smektala R, Endres HG, Dasch B, et al. The effect of time-to-surgery on outcome in elderly patients with proximal femoral fractures. *BMC Musculoskelet Disord*. 2008;9:171. [CrossRef]