

Impact of Delirium on Short-term Prognosis in Geriatric Patients with Hip Fracture

Shuai An

Xuanwu Hospital

Jingwei Wu

Xuanwu Hospital

Mingli Feng (✉ fengmingli6666@163.com)

Capital Medical University Xuan Wu Hospital

Zheng Li

Xuanwu Hospital

Zonghan Li

Xuanwu Hospital

Jingbo Cheng

Xuanwu Hospital

Guanglei Cao

Xuanwu Hospital

Limin Liu

Xuanwu Hospital

Shibao Lu

Xuanwu Hospital

Research article

Keywords: Delirium, Early prognosis, Hip fracture, Mortality, Older adult

Posted Date: August 21st, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-55975/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: To explore the effect of delirium on postoperative early prognosis of geriatric patients with hip fracture.

Methods: According to whether postoperative delirium (POD) appeared in elderly patients with hip fracture, all cases were divided into two groups: delirium and non-delirium. General parameters, operative parameters, length of stay (LOS), and perioperative complications were recorded. Recurrent fracture, new stroke, and mortality within 1 year postoperatively were followed up and compared between the two groups.

Results: Of 358 cases, 55 (15.4%) developed delirium. Compared with the non-delirium group, the delirium group had longer operative times ($P=0.031$); increased platelet ($P=0.002$) and C-reactive protein ($P<0.001$) levels; and reduced hemoglobin ($P<0.001$), calcium ($P=0.040$), albumin ($P<0.001$), prealbumin ($P<0.001$), and total cholesterol ($P=0.019$) levels. Complications occurred to some extent in 196 cases (54.7%). In the delirium group, complication rates of pulmonary infection ($P=0.005$), hypoalbuminemia ($P<0.001$), electrolyte disorder ($P<0.001$), dyspepsia ($P=0.027$), bedsore ($P=0.012$) and anemia ($P=0.007$) were higher. In addition, LOS was significantly longer (15.71 ± 4.72 vs 14.00 ± 5.30 days; $P=0.026$) in the delirium group. Within 1 year postoperatively, 31 individuals (8.7%) had died, 13 were treated for recurrent fracture, and 42 had a new stroke. In the delirium group, mortality within 1 year postoperatively was higher (27.3% vs 5.3%, $P<0.001$).

Conclusions: The morbidity of POD is high in geriatric patients with hip fractures. There was longer surgery delay, higher complication rate, longer LOS, and increased mortality in the delirium group. Early intervention of POD has important clinical significance.

Background

Hip fracture in elderly patients is one of the most common osteoporotic fractures. As society is increasingly aging, the amount of hip fractures is increasing¹. Patients with hip fractures are typically older adult and, therefore, often have complications from several diseases, decreased cardiopulmonary and other systemic functions, lower compensatory capability, and more complications during hospital stay; indeed, clinically this kind of fracture was called the 'last fracture in a person's life'. Past studies have indicated that the mortality of hip fracture in elderly patients was 15–33% within 1 year postoperatively, and half of all patients endured disabling outcomes^{2, 3}. Postoperative new stroke and recurrent fracture were the main causes of failure to return to normal life for patients with hip fractures. Thus, to increase the quality and value of life for geriatric patients, it is very important to analyze risk factors for poor prognosis postoperatively.

Postoperative delirium (POD) is a common clinical manifestation that occurs in 13–51% of elderly patients with hip fractures^{4, 5}. Several studies have demonstrated a correlation between POD and length

of stay (LOS), as well as hospital costs⁶⁻⁸. Recently Hamilton et al. reported that POD could increase the postoperative mortality of patients who underwent non-cardiac surgery⁹. However, studies focusing on possible relationships between POD and short-term prognosis in geriatric patients with hip fractures are lacking.

In this study, we collected the clinical statistics of elderly patients with hip fractures treated in our hospital, with the aim of analyzing potential correlations between POD and short-term prognosis, such as LOS, early complications during the hospital stay, and postoperative mortality.

1. Methods

1.1 Patient selection and grouping

Inclusion criteria: (1) age ≥ 65 years, (2) femoral intertrochanteric fracture or femoral neck fracture, (3) low energy injury, (4) single hip fracture, and (5) receiving surgery treatment. Exclusion criteria: (1) car accident or other high energy injury; (2) open wound injury, pathological fracture, or old fracture (more than 3 weeks); (3) receiving conservative treatment without surgical treatment; or (4) incomplete data or failure to follow up.

This study was approved by the Ethics Committee of Xuan Wu Hospital, Capital Medical University (Beijing, China). A total of 378 cases of geriatric hip fracture were collected from January 2016 to December 2018. Among all cases, two resulted from car accidents, two occurred with pathological fractures, two occurred with old fractures, five were treated with conservative treatments, and ten cases failed to follow up; all these cases were excluded according to the exclusion criteria. The remaining 358 cases were enrolled in this study, of which 121 patients were male and 237 patients were female. Ages ranged from 65 to 99 years, with an average of 79.67 ± 7.09 years. The time from injury to operation ranged between 1 and 20 days, with an average time of 6.86 ± 3.24 days. One hundred seventy-nine cases were injured on the left side, while 179 cases were injured on the right side. One hundred forty-seven cases occurred with femoral neck fracture, while 211 cases occurred with intertrochanteric fracture. With regard to treatments, 223 cases underwent internal fixation, 211 cases were fixed with an intramedullary nail, 135 cases were treated with arthroplasty, and 12 cases adopted a cannulated screw.

Groups were divided according to whether POD occurred. According to the Confusion Assessment Method (CAM) described in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), all elderly patients with hip fracture were screened and evaluated¹⁰ by a group of clinicians who had been trained. Assessment items included: (1) acute onset and fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered level of consciousness. The diagnosis of delirium by CAM requires the presence of features 1, 2, and either 3 or 4. All patients were divided into two groups: delirium (55 cases) and non-delirium (303 cases).

1.2 Data collection and follow up methods

The following data of each case were recorded and collected. (1) General information and operative data such as gender, age, body mass index, preoperative coexisting diseases (e.g., hypertension, diabetes mellitus, chronic obstructive pulmonary disease, coronary heart disease, old myocardial infarction, old cerebral infarction, Parkinson's disease, hepatic dysfunction, and renal dysfunction), preoperative laboratory examination (e.g., blood routine, hepatic and renal function tests, coagulation test, inflammatory biomarkers), injury-to-operation time, American Society of Anesthesiologists (ASA) scale, type of anesthesia, type of operative, and operative time. (2) Length of stay: dates of the hospital stay. (3) Perioperative complications were checked and analyzed, such as pulmonary infection, deep venous thrombosis, urinary system infection, hypoproteinemia, electrolyte disorder, arthralgia, ankyloses, dyspepsia, bedsore, arrhythmia, cerebrovascular accident, multiorgan dysfunction, anemia. (4) All patients were followed up to record whether recurrent fracture, new stroke, or death occurred within 1 year by telephone or outpatient service after discharge.

1.3 Operative condition and perioperative management

The surgeons in charge of each patient had the qualifications of attending physician or above, and the capabilities of all doctors were comparable. All patients underwent routine examinations before treatment. Intraoperative spinal anesthesia was routinely used (only two patients underwent general anesthesia). Intertrochanteric fractures were treated with closed reduction and intramedullary nails. For non-displaced femoral neck fractures, hollow nails were used with internal fixation; whereas, displaced femoral neck fractures were treated with hip replacement. Antibiotics were given 30 minutes before surgery and within 1 day after surgery to prevent infection. Non-steroidal analgesia and low molecular-weight heparin anticoagulation were given during the perioperative period. Early functional training was started on the first day after surgery. All patients were prescribed vitamin D and calcium for bone protection at discharge.

1.4 Statistical method

Data were collected and processed using MS Excel and SPSS 19.0 software. Measurement data are expressed as mean \pm standard deviation. Comparisons between groups were performed using independent sample t-tests; counted data were analyzed by Chi-Square test. For non-normally distributed data, non-parametric tests were used. $P < 0.05$ was considered statistically significant.

2. Results

2.1 Comparison of general data in delirium and non-delirium groups

A total of 358 older adult hip fracture cases were enrolled in this study, of which 55 had POD, yielding an incidence of 15.4%. As shown in Table 1 and Table 2, there was no significant difference in gender, age, body mass index, fracture type, fixation method, number of comorbidities, ASA classification, or operation time between the two groups ($P > 0.05$). However, compared with the non-delirium group, the delirium group had a longer injury-to-operation time ($P = 0.031$); increased platelet counts ($P = 0.002$) and C-reactive protein levels ($P < 0.001$); and reduced levels of serum calcium ($P = 0.040$), albumin ($P < 0.001$), prealbumin ($P < 0.001$), and total cholesterol ($P = 0.019$).

Table 1
Comparison of two groups of general information

Variables	Non-delirium group(n = 303)	Delirium group (n = 55)	χ^2 / t	P value
Gender			0.191	0.646
male	101	20		
female	202	35		
Age(years)	79.40 ± 7.00	81.15 ± 7.45	-1.685	0.093
BMI(Kg/m ²)	22.89 ± 3.32	22.72 ± 4.35	0.278	0.782
Fracture type			3.848	0.054
Femoral neck fracture	131	16		
Femoral intertrochanteric fracture	172	39		
Fixing method			2.055	0.152
Internal fixation	184	39		
Joint replacement	119	16		
Number of comorbidities			3.602	0.608
None	74	9		
1 kind	107	25		
2 kinds	81	16		
3 kinds and more	41	5		
ASA scale			4.212	0.122
I	77	9		
II	170	30		
III	56	16		
Injury-to-operation time (days)	6.71 ± 3.13	7.73 ± 3.69	-2.162	0.031*
Operation time(hours)	1.48 ± 0.54	1.56 ± 0.56	-0.887	0.376

Table 2
Comparison of two groups of inspection items

Variable	Non-delirium group(n = 303)	Delirium group (n = 55)	χ^2 / t	P value
White blood cells($\times 10^9 / L$)	8.81 \pm 5.54	8.39 \pm 3.73	0.551	0.582
Hemoglobin(g/L)	119.61 \pm 20.76	103.01 \pm 22.27	5.394	< 0.001*
Platelets($\times 10^9 / L$)	188.31 \pm 62.80	224.44 \pm 78.86	-3.217	0.002*
Lymphocyte($\times 10^9 / L$)	1.33 \pm 0.63	1.19 \pm 0.55	1.542	0.124
Neutrophils($\times 10^9 / L$)	7.00 \pm 6.44	6.34 \pm 3.59	0.741	0.459
Creatinine(μ mol/L)	72.88 \pm 61.44	75.76 \pm 42.43	-0.334	0.739
Urea nitrogen(mmol/L)	10.05 \pm 31.13	10.55 \pm 20.36	-0.114	0.910
Blood calcium(mmol/L)	2.16 \pm 0.34	2.06 \pm 0.15	2.061	0.040*
Albumin(g/L)	37.50 \pm 3.78	31.55 \pm 4.50	10.434	< 0.001*
C-reactive protein(mg/L)	62.22 \pm 13.13	76.75 \pm 12.77	-7.581	< 0.001*
Prealbumin(g/L)	174.31 \pm 52.48	131.98 \pm 44.61	5.623	< 0.001*
Blood glucose(mmol/L)	6.88 \pm 2.41	6.61 \pm 2.87	0.744	0.457
Alanine aminotransferase (mmol/L)	14.03 \pm 9.28	16.36 \pm 18.33	-0.926	0.358
Aspartate aminotransferase(mmol/L)	2051 \pm 7.55	23.47 \pm 13.87	-1.545	0.128
γ -glutamyl transpeptidase(mmol/L)	27.95 \pm 44.38	28.49 \pm 47.55	-0.082	0.935
Activated partial thromboplastin time(s)	39.15 \pm 5.39	41.74 \pm 11.78	0.1.604	0.114
Thrombin time(s)	16.08 \pm 1.07	16.29 \pm 1.29	-1.313	0.190
INR	1.06 \pm 0.25	1.15 \pm 0.80	-0.841	0.404

Variable	Non-delirium group(n = 303)	Delirium group (n = 55)	χ^2 / t	P value
Fibrinogen(g)	6.27 ± 34.84	4.65 ± 1.29	0.346	0.730
Total cholesterol(mmol/L)	4.25 ± 0.92	3.93 ± 0.89	2.359	0.019*
Triglyceride(mmol/L)	1.11 ± 0.69	0.99 ± 0.41	1.307	0.192
D-dimer (mg/L)	2.57 ± 4.04	3.66 ± 4.46	-1.81	0.071

2.2 Comparison of complications and length of stay in delirium and non-delirium groups during hospitalization

Of all 358 cases, 196 had varying degrees of complications during hospitalization, yielding an incidence rate of 54.7%. As shown in Table 3, the incidence of complications during hospitalization was high in both groups. Compared with the non-delirium group, the delirium group had a higher incidence of pulmonary infection ($P = 0.005$), hypoalbuminemia ($P < 0.001$), electrolyte disturbance ($P < 0.001$), indigestion ($P = 0.027$), bedsores ($P = 0.012$), and anemia ($P = 0.007$). In addition, hospital stays (15.71 ± 4.72 vs 14.00 ± 5.30 days; $P = 0.026$) of the delirium group were significantly longer compared with the non-delirium group.

Table 3

Comparison of complications during hospitalization between delirium group and non-delirium group

Variable	Non-delirium group(n = 303)	Delirium group (n = 55)	χ^2 / t	<i>P</i> value
Pulmonary infection	61	21	8.588	0.005*
Deep vein thrombosis	18	4	0.143	0.705
Urinary tract infection	26	8	1.927	0.165
Hypoproteinemia	62	27	20.425	< 0.001*
Electrolyte disorders	9	11	25.595	< 0.001*
Arthralgia	0	1	5.525	0.154
Anchyloses	0	1	5.525	0.154
Dyspepsia	2	3	7.770	0.027*
Bed sore	1	3	11.064	0.012*
Arrhythmia	16	5	1.224	0.343
Cerebrovascular accident	4	3	4.151	0.076
Multiple organ failure	0	1	5.525	0.154
Anemia	57	20	8.494	0.007*

2.3 Comparison of mortality, recurrent fracture, and new stroke rates within 1 year after surgery between the two groups

As shown in Table 4, in this study, 31 elderly patients died within 1 year after operation for their hip fracture, accounting for 8.7% of the total number of cases. There were 13 cases of postoperative fractures, accounting for 3.6% of the total number of cases. In addition, 42 cases of postoperative stroke occurred, accounting for 11.7% of the total number of cases. Compared with the non-delirium group, the mortality rate of the delirium group was significantly higher within 1 year (27.3% vs 5.3%, $P < 0.001$).

Table 4
Comparison of mortality, recurrent fracture rate, and new stroke rate within 1 year after delirium and non-delirium groups

Variable	Non-delirium group(n = 303)	Delirium group (n = 55)	χ^2 / t	P value
Death	16	15	32.194	< 0.001*
Recurrent fracture	13	0	2.449	0.232
New stroke	36	6	0.042	0.837

3. Discussion

Compared with some research hotspots such as deep vein thrombosis, pulmonary embolism, and cardiovascular and cerebrovascular diseases of the lower extremities, POD is a common phenomenon, but it is easily ignored by orthopedic surgeons in elderly patients with hip fractures. Probably because POD is often an acute transient abnormality, resulting in missed diagnosis and misdiagnosis, which may lead to patients not receiving timely, reasonable, and effective intervention^{6, 11-13}. In this study, we found that POD may be associated with a series of early adverse prognoses. Compared with the non-delirium group, the delirium group was more likely to have perioperative complications and the incidence of pulmonary infection, hypoalbuminemia, electrolyte disturbance, indigestion, bedsores, and anemia was higher. In addition, the length of stay was longer in the delirium group. Moreover, the mortality rate was 27.3% in the delirium group within one year after operation, which was five times that of the non-delirium group.

Our results are similar to those of previous studies. Hamilton et al.⁹ reviewed 34 of 4968 screened citations and found that delirium was associated with a four-fold increase in the risk of death. Mosk et al.⁷ reported that delirium was correlated with a longer hospital stay, increased associated with complications, institutionalization, and 6-month mortality by observing 566 patients with hip fractures who were over the age of 70. Bellelli et al.¹⁴ reported that hypoactivity and mixed POD were associated with increased 6-month mortality risk. They observed 571 patients in which the morbidity of delirium was 38.5%, whereas the mortality rates of non-delirium and delirium groups separately were 8.3% and 24.1%, respectively. Bai et al.⁴ enrolled a total of 6288 patients and reported the prevalence of POD was 28% (23%–34%). They found that approximately one-fourth of patients undergoing hip fracture surgery went on to develop POD, and delirium increased both short-term and long-term mortality in these patients. Recently, Bielza et al.⁵ observed 383 patients with hip fracture who were over 70 years of age and found that 212 patients had POD; they found no correlation between delirium and mortality, walking ability, length of stay, or clinical complications. However, the in-hospital mortality of non-delirium and delirium groups was 4.6% and 3.3%, which is obviously lower than previously reported mortality rates of geriatric hip fractures. This difference may be related to the relatively short duration of their observation period, as

they only collected data during the hospital stay. Therefore, there is a positive correlation between delirium and complications, as well as mortality, in our study and several similar studies. According to our results, early detection, early diagnosis, and early treatment of POD are very important and have positive clinical significance for reducing perioperative complications and the length of hospital stays, and improving mortality.

POD is correlated with early postoperative poor prognosis. The underlying reason may be that POD is a manifestation of systemic inflammatory responses, not just local stress responses. In 2008, Van Munster et al. first proposed that the systemic inflammatory response plays an important role in the occurrence of delirium¹⁵. Subsequent research on the mechanism of clinical POD caused by systemic inflammatory response has shown that acute peripheral inflammatory stimuli (such as infection, surgery, or trauma) can induce activation of parenchymal cells to promote the expression of proinflammatory cytokines (such as tumor necrosis factor, interleukin 6, and interleukin 1 β) and chemokines (such as monocyte chemoattractant protein 1) in the central nervous system, which causes destruction of the blood-brain barrier and subsequent neuron and synaptic dysfunction, resulting in delirium¹⁶. According to the results of this study, blood platelet counts and C-reactive protein levels were higher in patients with POD; whereas, hemoglobin, blood calcium, albumin, prealbumin, and total cholesterol levels were lower. These results indicate that delirium is indeed related to systematic inflammation, coagulation changes, and nutritional status of the whole body, not just local manifestations of the nervous system. In addition, Lee et al.¹⁷ found that about 30.2% (70 cases) of older adult hip fracture patients had delirium after surgery, of which 20% (14 cases) continued to experience delirium 4 weeks after surgery, indicating that not all delirium is temporary. Indeed, it may sometimes appear to be continuous until the patient's whole-body condition is adjusted. Therefore, POD needs to be treated as soon as possible to be corrected in time. Previous studies reported that delirium results from the combined effects of environmental, pathological, and physiological factors^{6, 11, 12}. Thus, early treatment should not just be symptomatic use of antipsychotic drugs such as haloperidol, olanzapine, and aripiprazole, but should also involve etiological treatments to reduce pain and suffering, correct hypoproteinemia and anemia, restore water and electrolyte balance, provide adequate oxygen inhalation and nutritional support, ensure good sleep, and allow patients to carry out early functional exercises.

In addition, early surgery may be an important measurement to prevent delirium and reduce mortality. The results of this study showed that the delirium group had a longer injury-to-surgery time than the non-delirium group. Pioli et al.¹⁸ considered the delay of surgery to be a risk factor for delirium. For older adult hip fracture patients with mild to moderate cognitive impairment, early surgery should be one of the preoperative goals. Other scholars have reported that early surgical treatment, epidural anesthesia, and a shortened hospital stay can reduce mortality following hospitalization of elderly patients with hip fractures^{3, 19, 20}. Therefore, in view of the characteristics of hip fractures in the older adult, active development of geriatric wards, multidisciplinary cooperation, and shortening the waiting time for surgery will help reduce POD and improve the early prognosis of patients.

This study has three limitations. First, although the gold standard for diagnosis of delirium, the CAM assessment, was used in this study and determined by individuals qualified as associate chief physician or above, the core symptoms of delirium are difficult to define and clinical symptoms, severity, and progression, are difficult to identify. As such, the CAM diagnosis method is based on the subjective judgment of the clinician and not quantitative scores¹⁰, so there is a certain degree of subjective bias. Second, a valid malnutrition diagnostic measure (eg MNA / MNA-SF) was not conducted in this study. In addition, as the duration, classification, and severity of delirium were not observed in this study, a prospective multicenter cohort study will be used for further analysis.

4. Conclusion

POD has a higher incidence in older adult hip fracture patients. Compared with the non-delirium group, the delirium group had a longer waiting time before surgery, was more prone to perioperative complications, had a longer hospital stay, and had a higher mortality rate within 1 year. Thus, early detection, early diagnosis, and early treatment of delirium after surgery have important clinical significance.

Abbreviations

POD: postoperative delirium; LOS: length of stay; CAM: Confusion Assessment Method; ASA: American Society of Anesthesiologists

Declarations

Acknowledgements

We thank Liwen Bianji, Edanz Group China (www.liwenbianji.cn/ac), for editing the English text of a draft of this manuscript.

Authors' contributions

S.A. conceived the experiment, S.A., J.W. and Z.L. conducted the experiment, M.F., J.C., G.C., L.L. and S.L. analyzed the results. S.A. and Z.L. wrote the draft of manuscript. All authors reviewed the manuscript.

Funding

Xuanwu Hospital Funds XWJL-2019033

Capital's Funds for Health Improvement and Research CFH 2020-4-2018

The funders were not involved in the collection, analyses and interpretation of data, in the writing or in the decision to submit the manuscript.

Availability of data and materials

The datasets used and analyzed in the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by Xuan Wu Hospital Ethical Committee. Due to the retrospective nature of the study, the need for informed consent was waived.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Author details

Department of Orthopedics, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

References

1. Chen M, Zhang Y, Du Y, et al. Epidemiological and clinical study of hip fracture in hospitalized elderly patients in Shanghai, China. *ARCH OSTEOPOROS*. 2019;14:37.
2. Lin X, Xiong D, Peng YQ, et al. Epidemiology and management of osteoporosis in the People's Republic of China: current perspectives. *CLIN INTERV AGING*. 2015;10:1017–33.
3. Yoo MS, Zhu S, Jiang SF, et al. Association of Reversal of Anticoagulation Preoperatively on 30-Day Mortality and Outcomes for Hip Fracture Surgery. *AM J MED* 2020: [Epub ahead of print].
4. Bai J, Liang Y, Zhang P, et al. Association between postoperative delirium and mortality in elderly patients undergoing hip fractures surgery: a meta-analysis. *OSTEOPOROSIS INT* 2019: [Epub ahead of print].
5. Bielza R, Zambrana F, Fernández De La Puente E, et al. Impact of delirium on short-term outcomes in hip fracture patients under a program of approach to delirium. *GERIATR GERONTOL INT* 2019: [Epub ahead of print].

ahead of print].

6. Slor CJ, Witlox J, Adamis D, et al. The trajectory of C-reactive protein serum levels in older hip fracture patients with postoperative delirium. *Int J Geriatr Psychiatry*. 2019;34:1438–46.
7. Mosk CA, Mus M, Vroemen JP, et al. Dementia and delirium, the outcomes in elderly hip fracture patients. *CLIN INTERV AGING*. 2017;12:421–30.
8. Radinovic K, Markovic-Denic L, Dubljanin-Raspopovic E, Marinkovic J, Milan Z, Bumbasirevic V. Estimating the effect of incident delirium on short-term outcomes in aged hip fracture patients through propensity score analysis. *GERIATR GERONTOL INT*. 2015;15:848–55.
9. Hamilton GM, Wheeler K, Di Michele J, Lalu MM, Mclsaac DI. A Systematic Review and Meta-analysis Examining the Impact of Incident Postoperative Delirium on Mortality. *ANESTHESIOLOGY*. 2017;127:78–88.
10. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegal AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *ANN INTERN MED*. 1990;113:941–48.
11. Shin JE, Kyeong S, Lee JS, et al. A personality trait contributes to the occurrence of postoperative delirium: a prospective study. *BMC PSYCHIATRY*. 2016;16:371.
12. Krogseth M, Watne LO, Juliebo V, et al. Delirium is a risk factor for further cognitive decline in cognitively impaired hip fracture patients. *Arch Gerontol Geriatr*. 2016;64:38–44.
13. Choi YH, Kim DH, Kim TY, Lim TW, Kim SW, Yoo JH. Early postoperative delirium after hemiarthroplasty in elderly patients aged over 70 years with displaced femoral neck fracture. *CLIN INTERV AGING*. 2017;12:1835–42.
14. Bellelli G, Carnevali L, Corsi M, et al. The impact of psychomotor subtypes and duration of delirium on 6-month mortality in hip-fractured elderly patients. *INT J GERIATR PSYCH*. 2018;33:1229–35.
15. van Munster BC, Korevaar JC, Zwinderman AH, Levi M, Wiersinga WJ, De Rooij SE. Time-course of cytokines during delirium in elderly patients with hip fractures. *J AM GERIATR SOC*. 2008;56:1704–09.
16. Wang Y, Shen X. Postoperative delirium in the elderly: the potential neuropathogenesis. *AGING CLIN EXP RES*. 2018;30:1287–95.
17. Lee KH, Ha YC, Lee YK, Kang H, Koo KH. Frequency, risk factors, and prognosis of prolonged delirium in elderly patients after hip fracture surgery. *Clin Orthop Relat Res*. 2011;469:2612–20.
18. Pioli G, Bendini C, Giusti A, et al. Surgical delay is a risk factor of delirium in hip fracture patients with mild-moderate cognitive impairment. *AGING CLIN EXP RES*. 2019;31:41–7.
19. Sieber FE, Neufeld KJ, Gottschalk A, et al. Effect of Depth of Sedation in Older Patients Undergoing Hip Fracture Repair on Postoperative Delirium: The STRIDE Randomized Clinical Trial. *JAMA SURG*. 2018;153:987–95.
20. Bai J, Zhang P, Liang X, Wu Z, Wang J, Liang Y. Association between dementia and mortality in the elderly patients undergoing hip fracture surgery: a meta-analysis. *J ORTHOP SURG RES*.

