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著者別名	安部 哲哉, 山崎 正志
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Kazuyoshi Kobayashi, MD¹, Shiro Imagama, MD¹, Kei Ando, MD¹, Naoki Ishiguro, MD¹, Masaomi Yamashita, MD², Yawara Eguchi, MD³, Morio Matsumoto, MD⁴, Ken Ishii, MD⁴, Tomohiro Hikata, MD⁴, Shoji Seki, MD⁵, Hidetomi Terai, MD⁶, Akinobu Suzuki, MD⁶, Koji Tamai, MD⁶, Masaaki Aramomi, MD⁷, Tetsuhiro Ishikawa, MD⁷, Atsushi Kimura, MD⁸, Hirokazu Inoue, MD⁸, Gen Inoue, MD⁹, Masayuki Miyagi, MD⁹, Wataru Saito, MD⁹, Kei Yamada, MD¹⁰, Michio Hongo, MD¹¹, Yuji Matsuoka, MD¹², Hidekazu Suzuki, MD¹², Atsushi Nakano, MD¹³, Kazuyuki Watanabe, MD¹⁴, Hirotaka Chikuda, MD¹⁵, Junichi Ohya, MD¹⁵, Yasuchika Aoki, MD¹⁶, Masayuki Shimizu, MD¹⁷, Toshimasa Futatsugi, MD¹⁷, Keihiro Mukaiyama, MD¹⁷, Masaichi Hasegawa, MD¹⁸, Katsuhito Kiyasu, MD¹⁹, Haku Iizuka, MD²⁰, Yoichi Iizuka, MD²⁰, Ryoichi Kobayashi, MD²⁰, Kotaro Nishida, MD²¹, Kenichiro Kakutani, MD²¹, Hideaki Nakajima, MD²², Hideki Murakami, MD²³, Satoru Demura, MD²³, Satoshi Kato, MD²³, Katsuhito Yoshioka, MD²³, Takashi Namikawa, MD²⁴, Kei Watanabe, MD^{25,26}, Kazuyoshi Nakanishi, MD²⁷, Yukihiro Nakagawa, MD²⁸, Mitsunori Yoshimoto, MD²⁹, Hiroyasu Fujiwara, MD³⁰, Norihiro Nishida, MD³¹, Yasuaki Imajo, MD³¹, Masashi Yamazaki, MD³², Masataka Sakane, MD³², Tetsuya Abe, MD³², Kengo Fujii, MD³², Takashi Kaito, MD³³, Takeo Furuya, MD³⁴, Sumihisa Orita, MD³⁴, and Seiji Ohtori, MD³⁴

¹ Nagoya University, Nagoya, Aichi, Japan

² Funabashi Central Hospital, Funabashi, Chiba, Japan

³ Shimoshizu National Hospital, Yotsukaido-shi, Chiba, Japan

⁴ Keio University, Shinjuku-ku, Tokyo, Japan

⁵ University of Toyama, Toyama-shi, Toyama, Japan

⁶ Osaka City University, Abeno-ku, Osaka, Japan

⁷ Sanmu Medical Center, Sanmu-shi, Chiba, Japan

⁸ Jichi Medical University, Shimotsuke-shi, Tochigi, Japan

⁹ Kitasato University, Sagami-hara-shi, Kanagawa, Japan

¹⁰ Kurume University, Kurume-shi, Fukuoka, Japan

¹¹ Akita University, Akita-shi, Akita, Japan

¹² Tokyo Medical University, Shinjuku-ku, Tokyo, Japan

¹³ Osaka Medical College, Takatsuki-shi, Osaka, Japan

¹⁴ Fukushima Medical University, Fukushima-shi, Fukushima, Japan

¹⁵ The University of Tokyo, Bunkyo-ku, Tokyo, Japan

¹⁶ Eastern Chiba Medical Center, Togane, Japan

¹⁷ Shinshu University, Matsumoto-shi, Nagano, Japan

¹⁸ Kyorin University, Mitaka-shi, Tokyo, Japan

¹⁹ Kochi University, Nankoku-shi, Kochi, Japan

²⁰ Gunma University, Maebashi-shi, Gunma, Japan

²¹ Kobe University, Kobe-shi, Hyogo, Japan

²² University of Fukui, Yoshida-gun, Fukui, Japan

²³ Kanazawa University, Kanazawa, Ishikawa, Japan

²⁴ Osaka City General Hospital, Miyakojima-ku, Osaka, Japan

²⁵ Niigata University, Niigata-shi, Niigata, Japan

²⁶ Sado General Hospital, Sado-shi, Niigata, Japan

²⁷ Hiroshima University, Hiroshima-shi, Hiroshima, Japan

²⁸ Wakayama Medical University, Wakayama-shi, Wakayama, Japan

²⁹ Sapporo Medical University, Sapporo-shi, Hokkaido, Japan

³⁰ Osaka-Minami Medical Center, Kawachinagano-shi, Osaka, Japan

³¹ Yamaguchi University, Ube, Yamaguchi, Japan

³² University of Tsukuba, Tsukuba, Ibaraki, Japan

³³ Osaka University, Suita, Osaka, Japan

³⁴ Chiba University, Chiba-shi, Chiba, Japan

Corresponding Author:

Shiro Imagama, Department of Orthopedic Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai Showa-ward, Aichi 466-8550, Japan.

Email: imagama@med.nagoya-u.ac.jp



Abstract

Study Design: Retrospective database analysis.

Objective: Spine surgeries in elderly patients have increased in recent years due to aging of society and recent advances in surgical techniques, and postoperative complications have become more of a concern. Postoperative delirium is a common complication in elderly patients that impairs recovery and increases morbidity and mortality. The objective of the study was to analyze postoperative delirium associated with spine surgery in patients aged 80 years or older with cervical, thoracic, and lumbar lesions.

Methods: A retrospective multicenter study was performed in 262 patients 80 years of age or older who underwent spine surgeries at 35 facilities. Postoperative complications, incidence of postoperative delirium, and hazard ratios of patient-specific and surgical risk factors were examined.

Results: Postoperative complications occurred in 59 of the 262 spine surgeries (23%). Postoperative delirium was the most frequent complication, occurring in 15 of 262 patients (5.7%), and was significantly associated with hypertension, cerebrovascular disease, cervical lesion surgery, and greater estimated blood loss ($P < .05$). In multivariate logistic regression using perioperative factors, cervical lesion surgery (odds ratio = 4.27, $P < .05$) and estimated blood loss ≥ 300 mL (odds ratio = 4.52, $P < .05$) were significantly associated with postoperative delirium.

Conclusions: Cervical lesion surgery and greater blood loss were perioperative risk factors for delirium in extremely elderly patients after spine surgery. Hypertension and cerebrovascular disease were significant risk factors for postoperative delirium, and careful management is required for patients with such risk factors.

Keywords

spine surgery, delirium, risk factors, complication, extremely elderly

Introduction

Postoperative delirium is a common complication of surgical procedures in the elderly and causes difficulty in postoperative care.^{1,2} The incidence of postoperative delirium ranges from 3.3% to 77%, with variation between studies depending on the patient population and surgeries.³⁻⁹ Delirium involves an acute generalized impairment of cognitive function that affects orientation, attention, memory, planning and organizational skills, and disturbs the sleep-awake cycle, thought process, perception, and activity level.¹⁰⁻¹² Acute delirium as a postoperative complication also increases morbidity and mortality and prolongs hospitalization.¹³⁻¹⁵ Prevention of delirium is important to reduce these problems and the associated costs, and thus there is a need for improved understanding of the risk factors to permit early diagnosis and effective management strategies.

The term *elderly* is generally accepted to indicate a chronological age of 65 years or older.¹⁶⁻²² The demand for spinal surgery in elderly persons has grown with aging of society and recent advances in surgical techniques and general anesthesia. Studies of postoperative complications after spine surgery have included extremely elderly patients aged over 80 years,²³⁻²⁶ and there are several reports on the incidence and risk factors for postoperative delirium associated with spine surgery.^{4,15,27-29} However, a study of delirium after spine surgery in extremely elderly patients aged 80 years or older and including surgeries for all spinal lesions has not been performed. Therefore, in this study, the frequency of delirium after spine surgery in patients aged 80 years or older and patient-specific and surgical risk factors were examined in a retrospective analysis of a multicenter database.

Materials and Methods

A retrospective multicenter survey was performed by JASA (Japan Association of Spine Surgeons with Ambition) in 262 patients aged 80 years or older who underwent spinal surgery at 35 centers. Institutional review board approval was obtained, and all data was obtained from medical records or nursing records. Of the patients, 122 were male and 140 were female. Age ranged from 80 to 91 years, with a mean of 82.7 years. None of the patients were receiving treatment for any specific form of dementia. The causative diseases were lumbar spinal canal stenosis due to spondylosis ($n = 132$), cervical spondylotic myelopathy ($n = 56$), lumbar spinal canal stenosis due to spondylolisthesis ($n = 21$), thoracic-lumbar compression fracture ($n = 19$), cervical ossification of the posterior longitudinal ligament ($n = 6$), pyogenic spondylitis ($n = 5$), and others ($n = 23$). The lesions were cervical ($n = 74$, 28%), thoracic ($n = 13$, 5%), and lumbar ($n = 175$, 67%). The mean operative time was 171 minutes, and the mean estimated blood loss (EBL) was 289 mL. There were 87 fusion surgeries with instrumentation.

Total intravenous anesthesia was administered during intraoperative spinal cord monitoring. The drugs administered were propofol (3-4 mg/mL), fentanyl (2 mg/kg), and vecuronium (0.12-0.16 mg/kg). Anesthesia was maintained using propofol (3-4 mg/mL), fentanyl (0.75-1 mg/kg/h), and vecuronium (0-0.04 mg/kg/h).

Delirium has 4 features—(1) acute onset and a fluctuating course, (2) inattention, (3) disorganization of thinking, and (4) an altered level of consciousness—and diagnosis requires the presence of features 1 and 2 and either 3 or 4.³⁰ Age,

Table 1. Details of Postoperative Complications.

Complication	Number of Cases
Delirium	15
Epidural hemorrhage	7
Surgical site infection	7
Urinary infection	6
Cerebral infarction	3
Transient muscle weakness	3
Renal dysfunction	2
C5 palsy	2
Systemic edema	2
Liver dysfunction	2
Respiration disorder	2
Others	8
Total	59

gender, previous spinal surgery, body mass index, disease duration, smoking status, drug use (nonsteroidal anti-inflammatory drugs, opioids, osteoporosis agents, and anticoagulants), comorbidities (hypertension, preexisting neoplasm, diabetes, and cerebrovascular disease), and operative factors (operative time, EBL, and fusion with instrumentation) were examined as potential risk factors for postoperative delirium.

For statistical analysis, differences between 2 groups were analyzed by Mann-Whitney *U* test, Student's *t* test, and those between 3 groups were analyzed by Kruskal-Wallis test. A multivariate logistic regression model was constructed using variables with $P < .05$ in univariate analysis. Multivariate hazard ratios are reported with 95% confidence intervals. Statistical analysis was performed using SPSS version 22 for Windows (IBM, Chicago, IL). $P < .05$ was considered to be significant in all analyses.

Results

Postoperative complications occurred in 59 of the 262 operations (23%) in 50 patients. The details are shown in Table 1. Delirium was most frequent, occurring in 15 patients (5.7%), including 7 men and 8 women. Delirium lasted from a few hours to 3 days, and medication for treatment was not used in all cases. Of the 15 delirium cases, 4 (27%) occurred in the intensive care unit (ICU) on the day of surgery and improved on the next day after leaving the ICU. Delirium was more frequent in patients with hypertension ($P < .01$) and cerebrovascular disease ($P < .05$), and in those with a cervical lesion ($P < .01$) and greater EBL ($P < .05$; Table 2). Delirium occurred after 8, 1, and 6 surgeries on the cervical, thoracic, and lumbar spine, respectively, and was significantly more frequent after cervical spine surgery ($P < .05$; Figure 1). In multivariate logistic regression using perioperative factors, cervical lesion surgery (odds ratio = 4.27, 95% confidence interval = 1.41-12.8; $P < .05$) and EBL ≥ 300 mL (odds ratio = 4.52, 95% confidence interval = 1.50-13.7; $P < .05$) were significantly associated with postoperative delirium (Table 3).

Discussion

Delirium is an acute confused state with alterations in attention and consciousness³¹ that develops in 5% to 52% of older patients hospitalized for medical reasons or surgery.³² The incidences of delirium are 7% to 14% after general surgery,^{6,33} 21% to 61% after hip surgery,³⁴ 13% to 41% after joint replacement surgery,^{9,35} and 7% to 77% after open-heart surgery.^{36,37} The different rates in each surgery cause a major problem in clinical management.

The incidence of delirium after spine surgery has ranged from 0.49% to 21% in 6 previous reports (Table 4). Imagama et al¹ reported an incidence of delirium of 0.49% in 1012 lumbar spine surgeries in a single-center study and concluded that postoperative psychotic symptoms occurred significantly more often in older patients. Fineberg et al²⁹ found an incidence of delirium of 8.4 per 1000 lumbar spine procedures in an analysis of the Nationwide Inpatient Sample database, with an increased incidence in older females with more comorbidities. Kawaguchi et al⁴ reported an incidence of delirium of 12.5% in patients over 70 years of age who underwent spine surgery, and 2 patients who developed postoperative delirium died during the follow-up period. Previous studies of postoperative delirium in spine surgery have included patients of all ages^{1,4,27-29} or have focused on particular surgical procedures,^{28,29,38} but none have examined all spinal lesions in extremely elderly patients.

In the current study, we focused on spine surgery in patients aged 80 years or older. In the ultra-aging society, the demand for spinal surgery in extremely elderly patients has grown and surgeries have increased in recent years.^{23,24} Thus, a study focused on extremely elderly patients is significant. In our series, delirium was the most common complication after spine surgery, and the comorbidity rates of hypertension and cerebrovascular disease were significantly higher in patients with delirium. Postoperative delirium in extremely elderly patients is relatively common and has been associated with significant increases in mortality, complications, length of hospital stay, and admission to a long care facility.³⁰ There is also strong evidence for an association of cerebrovascular disease with postoperative delirium.³⁹ Our findings are consistent with these previous results.

Delirium is an acute confused state with fluctuations in consciousness, memory, attention, perceptions, and behavior.^{29,33} In extremely elderly patients, postoperative delirium also includes hallucinations, illusions, anxiety, psychomotor agitation, and disorientation, but the condition might be silent and unnoticed, or misdiagnosed as depression.⁴⁰ The adverse effects of delirium include a prolonged hospital stay and a decline in walking ability and functional restoration, which lead to further postoperative complications and higher mortality within 1 year.⁴¹ Delirium following surgery affects readmission and discharge rates, and ultimately leads to high resource use.⁴² Symptoms are usually seen on the first or second postoperative day and are often worse at night. Recovery is common, but delirium may result in death at as high a rate as 20% to 30%.³¹

Table 2. Associations Between Categorical Variables and Postoperative Delirium.

Item	Perioperative Delirium (+) (n = 15)	Perioperative Delirium (-) (n = 247)	P
Demographic data			
Over 85 years of age, n (%)	5 (33%)	52 (21%)	NS
Female, n (%)	8 (53%)	132 (53%)	NS
Previous spinal surgery, n (%)	5 (33%)	42 (17%)	NS
BMI (kg/m ²), mean ± SD	24.0 ± 2.4	23.3 ± 3.4	NS
Disease duration (years), mean ± SD	5.0 ± 6.3	3.6 ± 5.1	NS
Smoking status, n (%)	0 (0%)	4 (2%)	NS
Drug use			
NSAIDs, n (%)	9 (60%)	113 (46%)	NS
Opioids, n (%)	3 (20%)	12 (5%)	NS
Osteoporosis agents, n (%)	4 (27%)	47 (19%)	NS
Anticoagulants, n (%)	3 (20%)	38 (15%)	NS
Comorbidities			
Hypertension, n (%)	10 (67%)	104 (42%)	<.01
Cerebrovascular disease, n (%)	3 (20%)	12 (5%)	<.05
Preexisting neoplasm, n (%)	4 (27%)	29 (12%)	NS
Diabetes, n (%)	5 (33%)	35 (14%)	NS
Perioperative factors			
Cervical lesion, n (%)	8 (53%)	60 (24%)	<.01
Operative time (minutes), mean ± SD	189 ± 133	170 ± 92	NS
Estimated blood loss (mL), mean ± SD	524 ± 766	268 ± 519	<.05
Use of instrumentation, n (%)	7 (47%)	77 (31%)	NS
Postoperative factors			
Epidural hemorrhage, n (%)	1 (7%)	6 (2%)	NS
Surgical site infection, n (%)	0 (0%)	7 (3%)	NS
Urinary infection, n (%)	1 (7%)	5 (2%)	NS
Cerebral infarction, n (%)	0 (0%)	3 (1%)	NS
Transient muscle weakness, n (%)	0 (0%)	3 (1%)	NS

Abbreviations: BMI, body mass index; NSAID, nonsteroidal anti-inflammatory drug; NS, not significant.

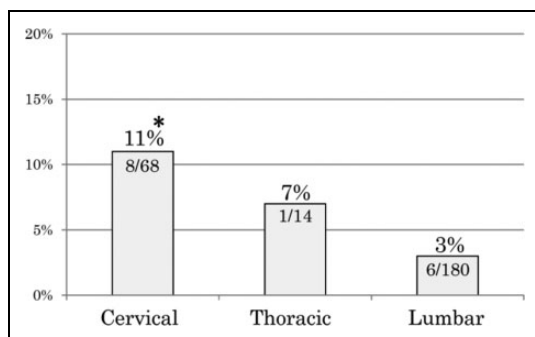


Figure 1. Relationship between surgical lesion and postoperative delirium. Delirium was significantly more frequent after cervical spine surgery. *P < .05.

There are several reports on risk factors for postoperative delirium, and the risk is multifocal. Predisposing factors include advanced age, history of alcohol/drug abuse, depression, psychotic disorders, neurological disorders, anemia, fluid/electrolyte disorders, and weight loss.²⁹ In addition, use of a stretcher or wheelchair at admission was found to be significantly higher in patients with delirium compared to those without delirium.⁴ This may indicate a poorer preoperative physical condition in patients who develop delirium, and postoperative delirium is common in older patients.

Table 3. Perioperative Risk Factors for Postoperative Delirium in a Multivariate Logistic Model^a.

	OR	95% CI	P
Cervical lesion surgery	4.27	1.41-12.8	.025
Blood loss ≥300 mL	4.52	1.50-13.7	.018

Abbreviations: OR, odds ratio; CI, confidence interval.

^aAll data was treated as continuous variables. The odds ratio is the increase in odds per unit increase in the predictor. Regression coefficients have been zero corrected.

Cerebral vascular disease is significantly associated with the incidence of delirium,³⁹ and hypoxic brain injury might cause postoperative delirium in those with cerebral vascular disease.⁴³ Preoperative exposure to stress, such as pain, immobilization, and psychological stress before surgery, may also cause delirium⁴ and such patients may have a poor postoperative prognosis.⁴⁴ Low serum albumin is a risk for postoperative complications and mortality,⁴⁵ and lower levels of hemoglobin and hematocrit may reduce oxygen supply to the brain, causing delirium.⁴⁶ Low oxygen saturation has also been associated with postoperative delirium.⁴⁷ Delirium in an ICU is frequently observed, with a prevalence of 46% to 70%.⁴⁸⁻⁵⁰ Delirium in the ICU is significantly increased by age and severity of illness,⁴⁹ and it may be associated with iatrogenic factors such as sedatives and analgesics causing brain dysfunction, in addition

Table 4. Summary of Studies on Postoperative Delirium.

Study	Year	Age Range	Mean Age (Years)	Surgical Lesion	Number of Cases	Incidence of Delirium	Risk Factors
Kawaguchi et al ⁴	2006	All ages	59.2	All lesions	341	3.8%	Low hemoglobin and hematocrit 1 day after surgery
Gao et al ²⁷	2008	All ages	48.2	All lesions	549	3.3%	Older age, diabetes mellitus, surgical history, blood transfusion >800 mL
Ushida et al ²⁸	2009	All ages	69.8	Cervical	122	21%	Over 70 years of age, hearing impairment
Lee et al ³⁸	2010	>60 years	73.5	Lumbar with fusion	217	13.6%	Cerebral vascular disease, low hemoglobin and hematocrit, poor nutritional status
Imagama et al ¹	2011	All ages	54.0	Lumbar	1012	0.49%	Elderly patients, longer operative time, greater EBL, and instrumentation surgery
Fineberg et al ²⁹	2013	All ages	55.1	Lumbar	578,457 (NIS database)	0.84%	History of alcohol/drug abuse, depression, psychotic disorders, anemia, weight loss
Present study	2016	≥80 years	82.7	All lesions	262	5.7%	Cervical lesion surgery, EBL ≥300 mL

Abbreviations: EBL, estimated blood loss; NIS, Nationwide Inpatient Sample.

to sepsis, postoperative cognitive dysfunction, and changes in biomarkers and neurotransmitters.⁴⁸

In our series, cervical spine surgery and EBL >300 mL were significant risk factors for delirium. In head and neck surgery, the rate of postoperative delirium is 17% to 36%.⁵¹⁻⁵⁵ Similarly, in cervical spine surgery, postoperative restriction is often necessary due to the risk of drain removal and prevention of excessive hematoma, and external fixation with a collar might also increase postoperative stress. Increased EBL might reduce albumin and cause anemia.^{4,27,38} Imagama et al also reported that greater EBL and longer operative time were significantly associated with postoperative complications.¹ The systemic excess capacity is poor in extremely elderly patients, and thus it is important to suppress intraoperative bleeding as much as possible.

Prevention of delirium is important for postoperative management since this condition can produce unexpected trauma and accidental drain removal. Early postoperative free movement wearing an orthosis may be effective for preventing delirium, along with drugs such as melatonin, haloperidol, donepezil, risperidone, and benzodiazepines⁵⁶⁻⁵⁹ and reduced use of methylprednisolone.²⁸ In our series, none of the 15 cases with delirium received methylprednisolone, and this drug was not routinely used in postoperative care. Delirium may also be prevented by normalization of circadian rhythm from a disordered state caused by multiple surgery-related factors. Such prevention in the extremely elderly may be important to avoid interference with postoperative rest and nursing. A prospective study is needed to evaluate preventive methods for postoperative delirium.

This study has several limitations. First, it was a retrospective study based on a data review that did not allow evaluation of preoperative severity. Second, the details of delirium were not available. Despite these limitations, postoperative delirium is of great concern in extremely elderly patients, and the results presented here provide important estimates of inpatient morbidity and mortality after spinal surgery. This is the first study

that revealed the risk factors for postoperative delirium after spine surgery in patients aged 80 years or older.

In conclusion, cervical lesion surgery and greater blood loss were found to be perioperative risk factors for postoperative delirium in extremely elderly patients, which suggests a need for careful surgical planning. Hypertension and cerebrovascular disease were significant factors for postoperative delirium. Early recognition and management of delirium based on identifiable risk factors may be useful for prevention, which may improve morbidity and delayed functional recovery.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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References

1. Imagama S, Kawakami N, Tsuji T, et al. Perioperative complications and adverse events after lumbar spinal surgery: evaluation of 1012 operations at a single center. *J Orthop Sci.* 2011;16:510-515.
2. Schmitt EM, Marcantonio ER, Alsop DC, et al. Novel risk markers and long-term outcomes of delirium: the successful aging after elective surgery (SAGES) study design and methods. *J Am Med Dir Assoc.* 2012;13:818.e1-e10.
3. Brauer C, Morrison RS, Silberzweig SB, Siu AL. The cause of delirium in patients with hip fracture. *Arch Intern Med.* 2000;160:1856-1860.
4. Kawaguchi Y, Kanamori M, Ishihara H, et al. Postoperative delirium in spine surgery. *Spine J.* 2006;6:164-169.
5. Morrison RS, Chassin MR, Siu AL. The medical consultant's role in caring for patients with hip fracture. *Ann Intern Med.* 1998;128:1010-1020.

6. Marcantonio ER, Goldman L, Orav EJ, Cook EF, Lee TH. The association of intraoperative factors with the development of postoperative delirium. *Am J Med.* 1998;105:380-384.
7. Gustafson Y, Brännström B, Berggren D, et al. A geriatric-anesthesiologic program to reduce acute confusional states in elderly patients treated for femoral neck fractures. *J Am Geriatr Soc.* 1991;39:655-662.
8. Williams-Russo P, Urquhart BL, Sharrock NE, Charlson ME. Post-operative delirium: predictors and prognosis in elderly orthopedic patients. *J Am Geriatr Soc.* 1992;40:759-767.
9. Rogers MP, Liang MH, Daltroy LH, et al. Delirium after elective orthopedic surgery: risk factors and natural history. *Int J Psychiatry Med.* 1989;19:109-121.
10. Dyer CB, Ashton CM, Teasdale TA. Postoperative delirium. A review of 80 primary data-collection studies. *Arch Intern Med.* 1995;155:461-465.
11. Parikh SS, Chung F. Postoperative delirium in the elderly. *Anesth Analg.* 1995;80:1223-1232.
12. Meagher DJ. Delirium: optimising management. *BMJ.* 2001;322:144-149.
13. Rockwood K. The occurrence and duration of symptoms in elderly patients with delirium. *J Gerontol.* 1993;48: M162-M166.
14. Rockwood K, Cosway S, Carver D, Jarrett P, Stadnyk K, Fisk J. The risk of dementia and death after delirium. *Age Ageing.* 1999;28:551-556.
15. Leslie DL, Zhang Y, Holford TR, Bogardus ST, Leo-Summers LS, Inouye SK. Premature death associated with delirium at 1-year follow-up. *Arch Intern Med.* 2005;165:1657-1662.
16. Deyo RA, Cherkin DC, Loeser JD, Bigos SJ, Ciol MA. Morbidity and mortality in association with operations on the lumbar spine. The influence of age, diagnosis, and procedure. *J Bone Joint Surg Am.* 1992;74:536-543.
17. Katz JN, Lipson SJ, Larson MG, McInnes JM, Fossel AH, Liang MH. The outcome of decompressive laminectomy for degenerative lumbar stenosis. *J Bone Joint Surg Am.* 1991;73:809-816.
18. Lee MJ, Konodi MA, Cizik AM, et al. Risk factors for medical complication after cervical spine surgery: a multivariate analysis of 582 patients. *Spine (Phila Pa 1976).* 2013;38:223-228.
19. Carreon LY, Puno RM, Dimar JR 2nd, Glassman SD, Johnson JR. Perioperative complications of posterior lumbar decompression and arthrodesis in older adults. *J Bone Joint Surg Am.* 2003;85:2089-2092.
20. Roebuck J. When does "old age begin? The evolution of the English definition. *J Social History.* 1979;12:416-428.
21. Gorman M. Development and the rights of older people. In: Randel J, German T, Ewing D, eds. *The Ageing and Development Report: Poverty, Independence and the World's Older People.* London, England: Earthscan; 1999:3-21.
22. Thane P. History and the sociology of ageing. *Soc Hist Med.* 1989;2:93-96.
23. Sciubba DM, Scheer JK, Yurter A, et al. Patients with spinal deformity over the age of 75: a retrospective analysis of operative versus non-operative management. *Eur Spine J.* 2016;25:2433-2441.
24. Wang MY, Green BA, Shah S, Vanni S, Levi AD. Complications associated with lumbar stenosis surgery in patients older than 75 years of age. *Neurosurg Focus.* 2003;14:e7.
25. Bydon M, Abt NB, De la Garza-Ramos R, et al. Impact of age on short-term outcomes after lumbar fusion: an analysis of 1395 patients stratified by decade cohorts. *Neurosurgery.* 2015;77:347-353.
26. Li G, Patil CG, Lad SP, Ho C, Tian W, Boakye M. Effects of age and comorbidities on complication rates and adverse outcomes after lumbar laminectomy in elderly patients. *Spine (Phila Pa 1976).* 2008;33:1250-1255.
27. Gao R, Yang ZZ, Li M, Shi ZC, Fu Q. Probable risk factors for postoperative delirium in patients undergoing spinal surgery. *Eur Spine J.* 2008;17:1531-1537.
28. Ushida T, Yokoyama T, Kishida Y, et al. Incidence and risk factors of postoperative delirium in cervical spine surgery. *Spine (Phila Pa 1976).* 2009;34:2500-2504.
29. Fineberg SJ, Nandyala SV, Marquez-Lara A, Oglesby M, Patel AA, Singh K. Incidence and risk factors for postoperative delirium after lumbar spine surgery. *Spine (Phila Pa 1976).* 2013;38:1790-1796.
30. Mouchoux C, Rippert P, Duclos A, et al. Impact of a multifaceted program to prevent postoperative delirium in the elderly: the CONFUCIUS stepped wedge protocol. *BMC Geriatr.* 2011;11:25.
31. Lipowski ZJ. Delirium (acute confusional states). *JAMA.* 1987;258:1789-1792.
32. Dasgupta M, Dumbrell AC. Preoperative risk assessment for delirium after noncardiac surgery: a systematic review. *J Am Geriatr Soc.* 2006;54:1578-1589.
33. Chrispal A, Mathews KP, Surekha V. The clinical profile and association of delirium in geriatric patients with hip fractures in a tertiary care hospital in India. *J Assoc Physicians India.* 2010;58:15-19.
34. Gustafson Y, Berggren D, Brännström B, et al. Acute confusional states in elderly patients treated for femoral neck fracture. *J Am Geriatr Soc.* 1988;36:525-530.
35. Hole A, Terjesen T, Breivik H. Epidural versus general anaesthesia for total hip arthroplasty in elderly patients. *Acta Anaesthesiol Scand.* 1980;24:279-287.
36. Breuer AC, Furlan AJ, Hanson MR, et al. Central nervous system complications of coronary artery bypass graft surgery: prospective analysis of 421 patients. *Stroke.* 1983;14:682-687.
37. Heller SS, Frank KA, Malm JR, et al. Psychiatric complications of open-heart surgery. A re-examination. *N Engl J Med.* 1970;283:1015-1020.
38. Lee JK, Park YS. Delirium after spinal surgery in Korean population. *Spine (Phila Pa 1976).* 2010;35:1729-1732.
39. Gosselt AN, Slooter AJ, Boere PR, Zaai IJ. Risk factors for delirium after on-pump cardiac surgery: a systematic review. *Crit Care.* 2015;19:346.
40. Tune LE. Postoperative delirium. *Int Psychogeriatr.* 1991;3:325-332.
41. Robertson BD, Robertson TJ. Postoperative delirium after hip fracture. *J Bone Joint Surg Am.* 2006;88:2060-2068.
42. Gleason LJ, Schmitt EM, Kosar CM, et al. Effect of delirium and other major complications on outcomes after elective surgery in older adults. *JAMA Surg.* 2015;150:1134-1140. doi:10.1001/jamasurg.2015.2606.

43. Wise MG. Delirium. In: Hales RE, Yudofsky SC, eds. *Textbook of Neuropsychiatry*. Washington, DC: American Psychiatric Press; 1987:89-105.
44. Schuurmans MJ, Duursma SA, Shortridge-Baggett LM, Clevers GJ, Pel-Littel R. Elderly patients with a hip fracture: the risk for delirium. *Appl Nurs Res*. 2003;16:75-84.
45. Rich MW, Keller AJ, Schechtman KB, Marshall WG Jr, Kouchoukos NT. Increased complications and prolonged hospital stay in elderly cardiac surgical patients with low serum albumin. *Am J Cardiol*. 1989;63:714-718.
46. Gustafson Y, Brännström B, Norberg A, Bucht G, Winblad B. Underdiagnosis and poor documentation of acute confusional states in elderly hip fracture patients. *J Am Geriatr Soc*. 1991;39:760-765.
47. Moller JT, Sennild I, Johannessen NW, et al. Perioperative monitoring with pulse oximetry and late postoperative cognitive dysfunction. *Br J Anaesth*. 1993;71:340-347.
48. Gunther ML, Morandi A, Ely EW. Pathophysiology of delirium in the intensive care unit. *Crit Care Clin*. 2008;24:45-65.
49. Mori S, Takeda JR, Carrara FS, Cohrs CR, Zanei SS, Whitaker IY. Incidence and factors related to delirium in an intensive care unit. *Rev Esc Enferm USP*. 2016;50:587-593.
50. Dessap AM, Roche-Campo F, Launay JM, et al. Delirium and circadian rhythm of melatonin during weaning from mechanical ventilation: an ancillary study of weaning trial. *Chest*. 2015;148:1231-1241.
51. Shah S, Weed H, He X, Agrawal A, Ozer E, Schuller DE. Alcohol-related predictors of delirium after major head and neck cancer surgery. *Arch Otolaryngol Head Neck Surg*. 2012;138:266-271.
52. Weed HG, Lutman CV, Young DC, Schuller DE. Preoperative identification of patients at risk for delirium after major head and neck cancer surgery. *Laryngoscope*. 1995;105:1066-1068.
53. Kunimatsu T, Misaki T, Hirose N, et al. Postoperative mental disorder following prolonged oral surgery. *J Oral Sci*. 2004;46:71-74.
54. Yamagata K, Onizawa K, Yusa H, Wakatsuki T, Yanagawa T, Yoshida H. Risk factors for postoperative delirium in patients undergoing head and neck cancer surgery. *Int J Oral Maxillofac Surg*. 2005;34:33-36.
55. Shiiba M, Takei M, Nakatsuru M, et al. Clinical observations of postoperative delirium after surgery for oral carcinoma. *Int J Oral Maxillofac Surg*. 2009;38:661-665.
56. Hanania M, Kitain E. Melatonin for treatment and prevention of postoperative delirium. *Anesth Analg*. 2002;94:338-339.
57. Seitz D, Gill SS. Perioperative haloperidol to prevent postoperative delirium. *J Am Geriatr Soc*. 2006;54:861.
58. Liptzin B, Laki A, Garb JL, Fingerhuth R, Krushell R. Donepezil in the prevention and treatment of post-surgical delirium. *Am J Geriatr Psychiatry*. 2005;13:1100-1106.
59. Prakanrattana U, Prapaitrakool S. Efficacy of risperidone for prevention of postoperative delirium in cardiac surgery. *Anaesth Intensive Care*. 2007;35:714-719.