



Comprehensive risk factor evaluation of postoperative delirium following major surgery: clinical data warehouse analysis

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Abstract

Background Postoperative delirium (POD) in older adults is a very serious complication. Due to the complexity of too many risk factors (RFs), an overall assessment of RFs may be needed. The aim of this study was to evaluate comprehensively the RFs of POD regardless of the organ undergoing operation, efficiently incorporating the concept of comprehensive big data using a smart clinical data warehouse (CDW).

Methods We reviewed the electronic medical data of inpatients aged 65 years or older who underwent major surgery between January 2010 and June 2016 at Hallym University Sacred Heart Hospital. The following six major operation types were selected: cardiac, stomach, colorectal, hip, knee, and spine. Clinical features, laboratory findings, perioperative variables, and medication history were compared between patients without POD and with POD.

Results Six hundred eighty-six of 3634 patients (18.9%) developed POD. In multivariate logistic regression analysis, common, independent RFs of POD were as follows (descending order of odds ratio): operation type ([hip] OR 8.858, 95%CI 3.432–22.863; $p = 0.000$; [knee] OR 7.492, 95%CI 2.739–20.487; $p = 0.000$; [spine] OR 6.919, 95%CI 2.687–17.815; $p = 0.000$; [colorectal] OR 2.037, 95%CI 0.784–5.291; $p = 0.144$; [stomach] OR 1.500, 95%CI 0.532–4.230; $p = 0.443$; [cardiac] reference), parkinsonism (OR 2.945, 95%CI 1.564–5.547; $p = 0.001$), intensive care unit stay (OR 1.675, 95%CI 1.354–2.072; $p = 0.000$), stroke history (OR 1.591, 95%CI 1.112–2.276; $p = 0.011$), use of hypnotics and sedatives (OR 1.307, 95%CI 1.072–1.594; $p = 0.008$), higher creatinine (OR 1.107, 95%CI 1.004–1.219; $p = 0.040$), lower hematocrit (OR 0.910, 95%CI 0.836–0.991; $p = 0.031$), older age (OR 1.053, 95%CI 1.037–1.069; $p = 0.000$), and lower body mass index (OR 0.967, 95%CI 0.942–0.993; $p = 0.013$). The use of analgesics (OR 0.644, 95%CI 0.467–0.887; $p = 0.007$) and antihistamines/antiallergics (OR 0.764, 95%CI 0.622–0.937; $p = 0.010$) were risk-reducing factors. Operation type with the highest odds ratio for POD was orthopedic surgery.

Conclusions Big data analytics could be applied to evaluate RFs in electronic medical records. We identified common RFs of POD, regardless of operation type. Big data analytics may be helpful for the comprehensive understanding of POD RFs, which can help physicians develop a general plan to prevent POD.

Keywords Delirium · Operation · Clinical data warehouse · Risk factor · Type of surgery · Parkinsonism

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Introduction

Postoperative delirium (POD) is a quite common surgical complication that presents predominantly in older people, with an incidence rate of 5% to 50% [1]. It is a serious complication, leading to loss of independence, prolonged hospitalization, deteriorated cognition, and elevated morbidity and mortality risk [1, 2].

Prevention of POD is critical, considering that if once POD has developed, treatment is challenging [1, 2]. The identification of risk factors (RFs) may be one of methods to understand the characteristics of POD and find a way for the prevention. Although the RFs for POD are well-known [1], studies on RFs

for POD are still being published. It might lead to increase the numbers of RFs [3]. Too many RFs can make it difficult to understand the characteristics of POD and to establish preventive strategies. One of the reasons that there were many RFs and RFs were various among studies may be that it is difficult to comprehensively evaluate all possible factors (i.e., epidemiologic, laboratory, perioperative factors, and medication history, etc.). To assess the level of each RF properly and to identify shared RFs, it is important to review medical records in detail for a number of potential RFs, but this can be a time-consuming task. Recently, medical records become rapidly digitized (i.e., known as electronic medical records [EMRs]), and big data analytics has been applied in the healthcare practices and research. It can provide a tool to manage and analyze structured and unstructured data quickly and precisely [4].

In addition, previous studies have done for a single surgical site only. There has been no direct comparison study regarding highly probable surgical site to result in POD, although the surgical sites are considered as a RF in review papers [5]. I assumed that knowing the shared RFs regardless of surgery type might help to understand the mechanism of POD and develop preventive strategies precisely and properly, because shared RFs might be much more closely related to core features in POD.

Therefore, the aim of the current study was to search for the common RFs of POD regardless of surgical sites by relying on further comprehensive big data using a smart clinical data warehouse (CDW). Hallym University Medical Center's smart CDW has been in use since 2016. The smart CDW, a solution for analyzing big data, is based on the QlikView Elite Solution (Qlik, Radnor, Pennsylvania, USA) [6]. Using this, it is possible to analyze fixed data (e.g., diagnoses, prescriptions, and laboratory findings) and EMR data in a narrative form (i.e., unstructured data).

Methods

Patients

We studied the electronic medical data of inpatients aged 65 years or older who underwent major surgery between January 2010 and June 2016 at Hallym University Sacred Heart Hospital in Anyang, Republic of Korea, and selected six major operation types after reviewing the literature about postoperative delirium: cardiac, stomach, colorectal, hip, knee, and spine, because surgeries themselves are so heterogeneous, we were afraid of bias if this study included as many as type of surgeries. Therefore, considering that previous studies of postoperative delirium was done in cardiac, stomach, colorectal, and orthopedic surgeries, I assumed that delirium was major concern in these surgeries than any others. Besides, if the patient had undergone multiple operations, only their

first operation was included in this study, since multiple operations were so divergent that there were several concerns in measurements and it would be a bias. Patients with POD were also operationally defined as people that demonstrated predetermined specific symptoms and signs of delirium in the consultation notes among all individuals who received psychiatric consultation after surgery. We made a set of word list about the specific symptoms and signs (Supplementary Table 1). Therefore, our smart CDW searched patients with these words in EMR. We excluded patients who presented with delirium prior to their operation and patients who received psychiatric consultation prior to surgery. By doing this, other psychiatric patients with similar symptoms to delirium can be excluded as much as possible. The study protocol was approved by the internal review board of our hospital.

Data collection

After a review of the literature, possible RFs for POD were investigated. The variables were demographics [e.g., age, sex, body mass index (BMI)]; previous medical history (e.g., hypertension, diabetes mellitus, tuberculosis, heart disease, stroke, cancer, hyperlipidemia, parkinsonism, dementia, depression, kidney disease, liver disease, insomnia); laboratory findings (e.g., hemoglobin, hematocrit, protein, total cholesterol, glucose, blood urea nitrogen, creatinine, uric acid); perioperative factors [e.g., operation type, estimated blood loss, anesthesia type, operation time, intensive care unit (ICU) stay]; and medications. Medication categories used the classifications already established in the Hallym order communication system; all classifications were made by our pharmaceutical team according to drug substance and characteristics (Supplementary Table 2).

Statistical analysis

Data are expressed as mean \pm standard deviation and frequency. Measurements were compared between patients without POD and those with POD. Statistical significance was evaluated by independent t-test and Chi-square test where appropriate. Multivariate logistic regression with backward elimination was performed on variables that showed with $p < 0.20$ in univariate logistic regression. We chose $p = 0.20$ as the threshold in multivariate analysis, as suggested elsewhere [7]. Values of $p < 0.05$ were regarded as significant. Statistical analysis was performed using IBM SPSS 22 Statistics (IBM Corp., Armonk, NY, USA).

Results

Of the studied 3634 patients, 686 (18.9%) developed delirium after surgery. The demographics, laboratory findings,

perioperative measurements, and medications of patients without POD and those with POD are summarized in Table 1. Many factors were associated with POD in univariate analyses.

Multivariate stepwise logistic regression analyses were performed to determine the independent risk factors of POD (Table 2). Age (OR 1.053, 95%CI 1.037–1.069; $p = 0.000$), BMI (OR 0.967, 95%CI 0.942–0.993; $p = 0.013$), stroke history (OR 1.591, 95%CI 1.112–2.276; $p = 0.011$), parkinsonism (OR 2.945, 95%CI 1.564–5.547; $p = 0.001$), hematocrit (OR 0.910, 95%CI 0.836–0.991; $p = 0.031$), creatinine (OR 1.107, 95%CI 1.004–1.219; $p = 0.040$), operation type ([hip] OR 8.858, 95%CI 3.432–22.863; $p = 0.000$; [knee] OR 7.492, 95%CI 2.739–20.487; $p = 0.000$; [spine] OR 6.919, 95%CI 2.687–17.815; $p = 0.000$; [colorectal] OR 2.037, 95%CI 0.784–5.291; $p = 0.144$; [stomach] OR 1.500, 95%CI 0.532–4.230; $p = 0.443$; [cardiac] reference), ICU stay (OR 1.675, 95%CI 1.354–2.072; $p = 0.000$), and use of hypnotics and sedatives (OR 1.307, 95%CI 1.072–1.594; $p = 0.008$) were independent RFs, whereas use of analgesics (e.g., tramadol, nefopam, and acetaminophen; OR 0.644, 95%CI 0.467–0.887; $p = 0.007$) and antihistamines/antiallergics (OR 0.764, 95%CI 0.622–0.937; $p = 0.010$) were risk-reducing factors.

Discussion

The existence of too many identified RFs of POD may hinder the establishment of a proper prevention strategy on the grounds that it is difficult to prioritize the most important RFs among them. Until now, the best way to prevent POD occurrence has been identification of RFs before surgery and proactive management [8]. In the present study, we identified common RFs of POD in major surgeries through a comprehensive evaluation using big data. Age, BMI, history of stroke, parkinsonism, hematocrit, creatinine, operation type, and ICU stay were all pinpointed as key RFs. With respect to medication, the use of hypnotics and sedatives was an RF, while, conversely, the use of analgesics (e.g., tramadol, nefopam) and antihistamines/antiallergics was an independent risk-reducing factor.

Advanced age is a well-known, clear RF of POD in various types of surgery. The mean age of patients with POD has been 70 years or older in most studies [9], and patients aged 65 years or older should be screened prior to surgery for the potential need of aggressive POD management [10]. Increased frailty due to a gradual increase in permanent damage of the nervous system due to aging and brain disorders may cause delirium in biological stress situations [10].

Lower BMI was reported to be a significant independent risk factor of POD, and it is thought to be associated with an undernutrition status [11]. Considering that BMI value was within the normal range in patients with delirium and was

above the normal range in patients without delirium in both ours and other studies [11], it is likely that overnutrition may be effective in prevention of delirium. However, more research is needed to determine whether BMI is a RF, because negative findings have also been reported [12–14].

Previous history of stroke is also a well-known RF of POD in cardiovascular surgery [10, 13, 15], but seems to be inconsistently known as an RF in noncardiovascular surgery including orthopedic and gastrointestinal surgery [11, 16]. These inconsistent findings may be due to the lack of proper research, because a number of nonvascular investigations did not consider history of previous stroke [12, 14, 17]. On the contrary, our study included various kinds of surgery and showed previous stroke history to be an independent RF for all. The precise role of previous stroke is poorly understood, but decreased brain function, cognitive impairment, and increased risk of cerebral hypoperfusion were assumed to be possible mechanisms [15, 16].

Parkinsonism was a significant RF of POD in our study and has been under-recognized in previous researches. A few studies have examined the relationship between delirium and Parkinson's disease (PD). PD has been suggested to be an RF for delirium [18], and delirium was frequently noted in hospitalized PD patients [19]. Recently, a nationwide database study showed that PD is a significant RF of POD in patients requiring total hip arthroplasty [20]. The mechanism was unknown, but alpha synucleinopathy was suggested to be associated with POD [21]. Because our study was retrospective, we could not differentiate parkinsonism disorders. However, it is presumed that the majority of patients with parkinsonism had PD, because patients with other parkinsonism disorders are not as likely to undergo surgery due to the poor prognosis of the diseases themselves.

Among preoperative routine laboratory tests, only hematocrit and creatinine were important RFs of POD in our study. Low pre- and postoperative hematocrit levels and low postoperative hemoglobin level were reported to be RFs of POD [22] and were postulated to be due to poor nutritional status [23] and poor oxygenation [24]. In our study, estimated blood loss was not different between patients without POD and those with POD, but preoperative hematocrit level was lower in patients with POD. We believe that these preoperative laboratory findings are important and that hematocrit and creatinine levels should be checked prior to surgery, because these are modifiable and can assist in preventing POD.

Among perioperative parameters, type of surgery and ICU stay were significant RFs of POD. Most studies have evaluated RF of POD in single-organ operations. One review article reported that emergency, orthopedics, and cardiac/vascular operations are the highest RFs for the occurrence of POD [5], while another described noncardiac thoracic and aortic aneurysm surgery as high RFs [1]. However, no specific analysis of the type of surgery as an RF for POD has been

Table 1 Characteristics of patients without and with postoperative delirium

Variables	patients without delirium (<i>n</i> = 2948, 81.1%)	patients with delirium (<i>n</i> = 686, 18.9%)	<i>p</i> value
Epidemiologic			
Age, years	74.6 ± 6.5	77.8 ± 6.7	0.000*
Women, <i>n</i> (%)	1642 (55.7)	444 (64.7)	0.000*
BMI ^a , kg/m ²	23.7 ± 4.1	22.7 ± 3.8	0.000*
HTN ^b , <i>n</i> (%)	1593 (54.9)	384 (56.1)	0.579
DM ^c , <i>n</i> (%)	670 (23.1)	172 (25.1)	0.270
Tuberculosis ^c , <i>n</i> (%)	71 (2.4)	13 (1.9)	0.482
Heart disease ^c , <i>n</i> (%)	233 (8.0)	79 (11.5)	0.004*
Stroke ^c , <i>n</i> (%)	130 (4.5)	61 (8.9)	0.000*
Cancer ^c , <i>n</i> (%)	198 (6.8)	47 (6.9)	0.933
Hyperlipidemia ^c , <i>n</i> (%)	157 (5.4)	29 (4.2)	0.250
Parkinsonism, <i>n</i> (%)	29 (1.0)	26 (3.8)	0.000*
Dementia, <i>n</i> (%)	62 (2.1)	43 (6.3)	0.000*
Depression, <i>n</i> (%)	0 (0.0)	0 (0.0)	–
Kidney disease, <i>n</i> (%)	50 (1.7)	16 (2.3)	0.267
Liver disease, <i>n</i> (%)	36 (1.2)	6 (9.0)	0.554
Insomnia ^d , <i>n</i> (%)	93 (3.2)	34 (5.0)	0.029
Laboratory			
Hemoglobin ^e , g/l	11.7 ± 1.9	11.1 ± 1.6	0.000*
Hematocrit ^f , %	34.9 ± 5.5	32.9 ± 4.9	0.000*
Protein ^g , g/dl	5.9 ± 1.1	5.6 ± 1.0	0.000*
Total cholesterol ^h , md/dl	145.7 ± 44.7	140.2 ± 41.1	0.002*
Glucose ⁱ , mg/dl	133.0 ± 42.7	131.3 ± 39.7	0.351
BUN ^g , mg/dl	16.3 ± 9.2	17.4 ± 9.7	0.010*
Creatinine ^j , mg/dl	0.8 ± 0.7	0.9 ± 1.1	0.108
Uric acid ^h , mg/dl	4.1 ± 1.7	3.9 ± 1.6	0.000*
Perioperative			
Operative type			0.000*
Cardiac, <i>n</i> (%)	79 (2.7)	6 (0.9)	
Stomach, <i>n</i> (%)	269 (9.1)	25 (3.6)	
Colorectal, <i>n</i> (%)	1127 (38.2)	109 (15.9)	
Hip, <i>n</i> (%)	720 (24.4)	344 (50.1)	
Knee, <i>n</i> (%)	203 (6.9)	39 (5.7)	
Spine, <i>n</i> (%)	550 (18.7)	163 (23.8)	
EBL ^k (ml)	629.3 ± 780.7	721.6 ± 630.2	0.004*
Anesthesia type^l			
General, <i>n</i> (%)	2377 (82.0)	534 (79.7)	0.167
Spinal/Epidural, <i>n</i> (%)	521 (18.0)	136 (20.3)	
Operation time (min)	169.3 ± 109.4	158.7 ± 105.8	0.001*
ICU stay, yes (%)	1402 (47.6)	374 (54.5)	0.001*
Use of medications			
CCBs, <i>n</i> (%)	583 (19.8)	155 (22.6)	0.102
Diuretics, <i>n</i> (%)	485 (16.5)	136 (19.8)	0.037*
Beta blockers, <i>n</i> (%)	480 (16.3)	132 (19.2)	0.070
ACE inhibitors, <i>n</i> (%)	200 (6.8)	54 (7.9)	0.319
ARBs, <i>n</i> (%)	495 (16.8)	129 (18.8)	0.216
Other antihypertensives, <i>n</i> (%)	290 (9.8)	76 (11.1)	0.325
Miscellaneous CV drugs, <i>n</i> (%)	58 (2.0)	15 (2.2)	0.653

Table 1 (continued)

Variables	patients without delirium (<i>n</i> = 2948, 81.1%)	patients with delirium (<i>n</i> = 686, 18.9%)	<i>p</i> value
Antidepressants, <i>n</i> (%)	534 (18.1)	137 (20.0)	0.275
Hypnotics & sedatives, <i>n</i> (%)	1188 (40.3)	321 (46.8)	0.002*
Antipsychotics, <i>n</i> (%)	238 (8.1)	80 (11.7)	0.004*
CNS stimulants, <i>n</i> (%)	19 (0.6)	5 (0.7)	0.794
Antimanic agents, <i>n</i> (%)	0 (0.0)	2 (0.3)	0.036*
Opioids, <i>n</i> (%)	1845 (62.6)	470 (68.5)	0.004*
Other analgesics (no NSADIs)	2485 (84.3)	604 (88.0)	0.013*
Skeletal muscle relaxants, <i>n</i> (%)	706 (23.9)	202 (29.4)	0.003*
Corticosteroids, <i>n</i> (%)	900 (30.5)	234 (34.1)	0.074
Antiplatelet agents, <i>n</i> (%)	531 (18.0)	126 (18.4)	0.826
Anticoagulants, <i>n</i> (%)	2160 (73.3)	564 (82.2)	0.000*
Antihyperlipidemic agents, <i>n</i> (%)	636 (21.6)	157 (22.9)	0.472
Antiparkinsonian agents, <i>n</i> (%)	69 (2.3)	12 (1.7)	0.392
Antihistamines/antiallergics, <i>n</i> (%)	1112 (37.7)	233 (34.0)	0.072
Antivertigos, <i>n</i> (%)	17 (0.6)	4 (0.6)	1.000
Genitourinary Smooth Muscle Relaxants, <i>n</i> (%)	139 (4.7)	26 (3.8)	0.359
H2 receptor antagonist, <i>n</i> (%)	1286 (43.6)	319 (46.5)	0.172

^a data missing from 277 patients (230 patients without delirium, the others with delirium), ^b data missing from 350 patients (48 patients without delirium, the others with delirium), ^c data missing from 50 patients (48 patients without delirium, the others with delirium), ^d data missing from 51 patients (48 patients without delirium, the others with delirium), ^e data missing from 15 patients without delirium, ^f data missing from 13 patients without delirium, ^g data missing from 14 patients without delirium, ^h data missing from 60 patients without delirium, ⁱ data missing from 21 patients without delirium, ^j data missing from 24 patients (22 patients without delirium, the others with delirium), ^k data missing from 65 patients (50 patients without delirium, the others with delirium), ^l data missing from 66 patients (50 patients without delirium, the others with delirium)

BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; BUN, blood urea nitrogen; EBL, estimated blood loss; ICU, intensive care unit; CCBs, Calcium channel blockers; ACE inhibitors: Angiotensin Converting Enzyme Inhibitors; ARBs, Angiotensin II Receptor Blockers; CV, cardiovascular; NSADIs, non-steroidal anti-inflammatory drugs

*Statistically significant ($p < 0.05$)

published. Because type of surgery was an important RF of POD, and major orthopedic surgery showed a higher odds ratio than did any of the other surgeries (e.g., gastrointestinal, cardiac) in our study (Table 2), we suggest that type of surgery should be considered when estimating the risk of POD and that medical staff members should be more cautious during major orthopedic surgeries.

In previous studies, medication type as an RF of POD was inconsistent, because a few studies investigated the effect of medications, while most studies that analyzed the POD risk regarding drugs did not categorize drugs before and after surgery [25]. Generally, polypharmacy, medications with anticholinergic activity, and psychotropic medications (e.g., benzodiazepines) are deemed to be RFs [1, 25, 26]. In one retrospective study, beta-blockers were reported to represent an RF of POD, while statins were a risk-reducing factor in vascular surgery [27], which also requires further study.

In the current study, use of hypnotics and sedatives was associated with development of POD. Although certain sedatives such as benzodiazepines are used to control

delirium, this use was also reported to be an RF of POD [28]. The mechanisms are unknown, and it was suggested to be the result of high affinity for the γ -aminobutyric acid receptor in the central nervous system, which may lead to the alteration of many neurotransmitter functions [29]. The reason that analgesics were a risk-reducing factor in our study may be associated with pain control, because pain is known to be an RF of POD [3]. The finding that tramadol was also a risk-reducing factor can be argued, because opioids and tramadol are known to be a strong RF of POD [30]. Notably, the contradictory results obtained may be due to the time of drug administration. We investigated only drugs that had been administered before surgery. Our results regarding antihistamines/antiallergics were also different from those of previous studies [28], but this requires further study because antihistamines have anticholinergic effects [31].

Our study has some limitations. First, we could not use standard delirium screening tool, but used operational definition of delirium to find patients with POD [32]. Second, it was a retrospective study, so not all patients were examined for

Table 2 Univariate and multivariate logistic regression analyses on risk factors for postoperative delirium

Variables	Univariate			Multivariate		
	<i>p</i> value	OR	95% CI	<i>p</i> value	OR	95% CI
Epidemiologic						
Age	0.000*	1.071	1.058-1.084	0.000*	1.053	1.037-1.069
Women	0.000*	1.459	1.228-1.734			
BMI	0.000*	0.932	0.910-0.955	0.013*	0.967	0.942-0.993
HTN	0.567	1.050	0.888–1.242			
DM	0.257	1.118	0.922–1.356			
Tuberculosis	0.396	0.772	0.425–1.403			
Heart disease	0.004*	1.495	1.141-1.958			
Stroke	0.000*	2.086	1.521-2.863	0.011*	1.591	1.112-2.276
Cancer	0.967	1.007	0.724–1.400			
Hyperlipidemia	0.214	0.774	0.516–1.160			
Parkinsonism	0.000*	3.965	2.320-6.777	0.001*	2.945	1.564-5.547
Dementia	0.000*	3.113	2.090-4.636	0.053	1.598	0.994–2.569
Depression	–	–	–			
Kidney disease	0.263	1.384	0.783–2.446			
Liver disease	0.446	0.714	0.300–1.701			
Insomnia	0.025*	1.581	1.058-2.364			
Laboratory						
Hemoglobin	0.000*	0.824	0.786-0.864	0.057	1.274	0.993–1.635
Hematocrit	0.000*	0.931	0.916-0.946	0.031*	0.910	0.836-0.991
Protein	0.000*	0.784	0.725-0.847			
Total cholesterol	0.003*	0.997	0.995-0.999			
Glucose	0.351	0.999	0.997–1.001			
BUN	0.008*	1.011	1.003-1.020			
Creatinine	0.047*	1.095	1.001-1.197	0.040*	1.107	1.004-1.219
Uric acid	0.000*	0.908	0.862-0.957			
Perioperative						
Operative type	0.000*			0.000*		
Cardiac				reference		
Stomach	0.669	1.224	0.485–3.088	0.443	1.500	0.532–4.230
Colorectal	0.579	1.273	0.543–2.988	0.144	2.037	0.784–5.291
Hip	0.000*	6.291	2.716-14.570	0.000*	8.858	3.432-22.863
Knee	0.043*	2.530	1.031-6.209	0.000*	7.492	2.739-20.487
Spine	0.002*	3.902	1.671-9.113	0.000*	6.919	2.687-17.815
EBL	0.013*	1.000	1.000			
Anesthesia type	0.163	1.162	0.941–1.435	0.052	0.768	0.588–1.002
Operation time	0.000*	0.999	0.998–1.000			
ICU stay	0.001*	1.322	1.119-1.562	0.000*	1.675	1.354-2.072
Use of medications						
CCBs	0.099	1.184	0.969–1.447			
Diuretics	0.035*	1.256	1.016-1.551			
Beta blockers	0.062	1.225	0.990–1.517			
ACE inhibitors	0.315	1.174	0.859–1.605			
ARBs	0.208	1.148	0.926–1.422			
Other antihypertensives,	0.331	1.142	0.874–1.492			
Miscellaneous CV drugs	0.713	1.114	0.627–1.977			
Antidepressants	0.259	1.128	0.915–1.391			

Table 2 (continued)

Variables	Univariate			Multivariate		
	<i>p</i> value	OR	95% CI	<i>p</i> value	OR	95% CI
Hypnotics & sedatives	0.002*	1.303	1.102–1.540	0.008*	1.307	1.072–1.594
Antipsychotics	0.003*	1.503	1.150–1.966			
CNS stimulants	0.806	1.132	0.421–3.042			
Antimanic agents	0.999	6.96E+09	0.000-			
Opioids	0.004*	1.301	1.089–1.554			
Other analgesics (no NSADIs)	0.013*	1.372	1.068–1.764	0.007*	0.644	0.467–0.887
Skeletal muscle relaxants	0.003*	1.325	1.102–1.594			
Corticosteroids	0.068	1.178	0.988–1.405			
Antiplatelet agents	0.828	1.024	0.826–1.270			
Anticoagulants	0.000*	1.687	1.364–2.085	0.080	1.274	0.972–1.672
Antihyperlipidemic agents	0.454	1.079	0.885–1.316			
Antiparkinsonian Agents	0.346	0.743	0.400–1.379			
Antihistamines/antiallergics	0.067	0.849	0.713–1.011	0.010*	0.764	0.622–0.937
Antivertigos	0.984	1.011	0.339–3.015			
Genitourinary Smooth Muscle Relaxants	0.296	0.796	0.519–1.220			
H2 receptor antagonist	0.172	1.123	0.951–1.327			

BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; BUN, blood urea nitrogen; EBL, estimated blood loss; ICU, intensive care unit; CCBs, Calcium channel blockers; ACE inhibitors: Angiotensin Converting Enzyme Inhibitors; ARBs, Angiotensin II Receptor Blockers; CV, cardiovascular; NSADIs, non-steroidal anti-inflammatory drugs

*Statistically significant ($p < 0.05$)

brain lesions by brain imaging, and the cause of parkinsonism was not differentiated. Third, emergent and nonemergent operations were not distinctly classified. Fourth, ICU stay was not divided between before and after surgery. Fifth, this study was conducted in one hospital, although it is a university tertiary hospital. Sixth, it would be worthy if we would deal patients with multiple operations and investigate the relationship between POD and the number of operations. Seventh, we restricted our analyses just to six kind of surgeries. Because our aim was to explore the common RFs of POD regardless of surgical sites, if we would include other kinds of surgeries (i.e., thoracic surgery, brain surgery, vascular surgery, neuro-radiological interventions, etc.), our research would be more valuable.

In conclusion, prevention is the best treatment of POD, and identification of RFs is essential, but too many factors were reported as RFs. More comprehensive data should be analyzed to simplify the number of RFs and to determine the ranking of RFs appropriately. It may take a long time to analyze such a large amount of data. Big data analytics may be efficient to solve this problem. We could evaluate almost all possible factors including demographics, medical history, perioperative findings, surgical sites, and medication history in a relatively short time. Our study showed that the RF evaluation was possible using the smart CDW, and big data analytics will help us to build simpler and more effective

prevention strategies by determining the correct ranking of all the possible RFs with much more multi-institutional database.

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Compliance with ethical standards

Conflicts of interest None.

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References

1. American Geriatrics Society Expert Panel on Postoperative Delirium in Older A (2015) Postoperative delirium in older adults: best practice statement from the American Geriatrics Society. *J Am Coll Surg* 220(2):136–148 e131. <https://doi.org/10.1016/j.jamcollsurg.2014.10.019>
2. Oh ES, Fong TG, Hshieh TT, Inouye SK (2017) Delirium in older persons: advances in diagnosis and treatment. *JAMA* 318(12):1161–1174. <https://doi.org/10.1001/jama.2017.12067>
3. Schenning KJ, Deiner SG (2015) Postoperative delirium in the geriatric patient. *Anesthesiol Clin* 33(3):505–516. <https://doi.org/10.1016/j.anclin.2015.05.007>

4. Belle A, Thiagarajan R, Soroushmehr SM, Navidi F, Beard DA, Najarian K (2015) Big data analytics in healthcare. *Biomed Res Int* 2015:370194–370116. <https://doi.org/10.1155/2015/370194>
5. McDaniel M, Brudney C (2012) Postoperative delirium: etiology and management. *Curr Opin Crit Care* 18(4):372–376. <https://doi.org/10.1097/MCC.0b013e3283557211>
6. Lee SH, Lee JJ, Kwon Y, Kim JH, Sohn JH (2017) Clinical implications of associations between headache and gastrointestinal disorders: a study using the Hallym smart clinical data warehouse. *Front Neurol* 8:526. <https://doi.org/10.3389/fneur.2017.00526>
7. Vittinghoff E, Glidden DV, Shiboski SC, McCulloch CE (2012) *Regression methods in biostatistics, linear, logistic, survival, and repeated measures models*, 2nd edn. Springer, San Francisco
8. Bettelli G, Neuner B (2017) Postoperative delirium: a preventable complication in the elderly surgical patient. *Monaldi Arch Chest Dis* 87(2):842. <https://doi.org/10.4081/monaldi.2017.842>
9. Aitken SJ, Blyth FM, Naganathan V (2017) Incidence, prognostic factors and impact of postoperative delirium after major vascular surgery: a meta-analysis and systematic review. *Vasc Med* 22(5):387–397. <https://doi.org/10.1177/1358863X17721639>
10. Inouye SK, Westendorp RGJ, Saczynski JS (2014) Delirium in elderly people. *Lancet* 383(9920):911–922. [https://doi.org/10.1016/s0140-6736\(13\)60688-1](https://doi.org/10.1016/s0140-6736(13)60688-1)
11. Huang J, Bin Abd Razak HR, Yeo SJ (2017) Incidence of postoperative delirium in patients undergoing total knee arthroplasty—an Asian perspective. *Ann Transl Med* 5(16):321. <https://doi.org/10.21037/atm.2017.06.40>
12. Chung KS, Lee JK, Park JS, Choi CH (2015) Risk factors of delirium in patients undergoing total knee arthroplasty. *Arch Gerontol Geriatr* 60(3):443–447. <https://doi.org/10.1016/j.archger.2015.01.021>
13. Galyfos GC, Geropapas GE, Sianou A, Sigala F, Filis K (2017) Risk factors for postoperative delirium in patients undergoing vascular surgery. *J Vasc Surg* 66(3):937–946. <https://doi.org/10.1016/j.jvs.2017.03.439>
14. Large MC, Reichard C, Williams JT, Chang C, Prasad S, Leung Y, DuBeau C, Bales GT, Steinberg GD (2013) Incidence, risk factors, and complications of postoperative delirium in elderly patients undergoing radical cystectomy. *Urology* 81(1):123–128. <https://doi.org/10.1016/j.urology.2012.07.086>
15. Lin Y, Chen J, Wang Z (2012) Meta-analysis of factors which influence delirium following cardiac surgery. *J Card Surg* 27(4):481–492. <https://doi.org/10.1111/j.1540-8191.2012.01472.x>
16. Guo Y, Jia P, Zhang J, Wang X, Jiang H, Jiang W (2016) Prevalence and risk factors of postoperative delirium in elderly hip fracture patients. *J Int Med Res* 44(2):317–327. <https://doi.org/10.1177/0300060515624936>
17. Oh ES, Li M, Fafowora TM, Inouye SK, Chen CH, Rosman LM, Lyketsois CG, Sieber FE, Puhan MA (2015) Preoperative risk factors for postoperative delirium following hip fracture repair: a systematic review. *Int J Geriatr Psychiatry* 30(9):900–910. <https://doi.org/10.1002/gps.4233>
18. Vardy ER, Teodorczuk A, Yarnall AJ (2015) Review of delirium in patients with Parkinson's disease. *J Neurol* 262(11):2401–2410. <https://doi.org/10.1007/s00415-015-7760-1>
19. Lubomski M, Rushworth RL, Tisch S (2015) Hospitalisation and comorbidities in Parkinson's disease: a large Australian retrospective study. *J Neurol Neurosurg Psychiatry* 86(3):324–330. <https://doi.org/10.1136/jnnp-2014-307822>
20. Newman JM, Sodhi N, Dalton SE, Khlopas A, Newman RP, Higuera CA, Mont MA (2018) Does Parkinson disease increase the risk of perioperative complications after Total hip arthroplasty? A Nationwide Database Study. *J Arthroplast* 33:S162–S166. <https://doi.org/10.1016/j.arth.2018.01.006>
21. Kim KH, Kang SY, Shin DA, Yi S, Ha Y, Kim KN, Sohn YH, Lee PH (2018) Parkinson's disease-related non-motor features as risk factors for post-operative delirium in spinal surgery. *PLoS One* 13(4):e0195749. <https://doi.org/10.1371/journal.pone.0195749>
22. Shi C, Yang C, Gao R, Yuan W (2015) Risk factors for delirium after spinal surgery: a meta-analysis. *World Neurosurg* 84(5):1466–1472. <https://doi.org/10.1016/j.wneu.2015.05.057>
23. Elsamadicy AA, Adogwa O, Ongele M, Sergesketter AR, Tarnasky A, Lubkin DET, Drysdale N, Cheng J, Bagley CA, Karikari IO (2018) Preoperative hemoglobin level is associated with increased health care use after elective spinal fusion (>=3 levels) in elderly male patients with spine deformity. *World Neurosurg* 112:e348–e354. <https://doi.org/10.1016/j.wneu.2018.01.046>
24. Gao R, Yang ZZ, Li M, Shi ZC, Fu Q (2008) Probable risk factors for postoperative delirium in patients undergoing spinal surgery. *Eur Spine J* 17(11):1531–1537. <https://doi.org/10.1007/s00586-008-0771-1>
25. Kassie GM, Nguyen TA, Kalisch Ellett LM, Pratt NL, Roughead EE (2017) Preoperative medication use and postoperative delirium: a systematic review. *BMC Geriatr* 17(1):298. <https://doi.org/10.1186/s12877-017-0695-x>
26. Bilotta F, Lauretta MP, Borozdina A, Mizikov VM, Rosa G (2013) Postoperative delirium: risk factors, diagnosis and perioperative care. *Minerva Anestesiol* 79(9):1066–1076
27. Katznelson R, Djaiani G, Mitsakakis N, Lindsay TF, Tait G, Friedman Z, Wasowicz M, Beattie WS (2009) Delirium following vascular surgery: increased incidence with preoperative beta-blocker administration. *Can J Anaesth* 56(11):793–801. <https://doi.org/10.1007/s12630-009-9148-0>
28. Clegg A, Young JB (2011) Which medications to avoid in people at risk of delirium: a systematic review. *Age Ageing* 40(1):23–29. <https://doi.org/10.1093/ageing/afq140>
29. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, Bernard GR, Ely EW (2006) Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology* 104(1):21–26
30. Son MJ, Choi SW, Hong YH, Lee HC, Yoo JH, Sung KH, Jang MU, Cho S-J, Kim JY, Kwon K-H, Kang SY (2017) Two cases of hallucination after administration of tramadol. *J Pain Auton Disord* 6(1):17–19
31. Lin KH, Chen YJ, Wei CF, Yen MH, Hsueh WC, Liao KC, Lu CL (2010) Prolonged withdrawal delirium in concomitant diphenhydramine and nefopam dependence: a case report. *Prog Neuro-Psychopharmacol Biol Psychiatry* 34(4):705–706. <https://doi.org/10.1016/j.pnpbp.2010.02.026>
32. Infante MT, Pardini M, Balestrino M, Finocchi C, Malfatto L, Bellelli G, Mancardi GL, Gandolfo C, Serrati C (2017) Delirium in the acute phase after stroke: comparison between methods of detection. *Neurol Sci* 38(6):1101–1104. <https://doi.org/10.1007/s10072-017-2832-x>