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Prevalence and Predictors of Delirium in Geriatrics undergoing Major Orthopedic Surgeries:aCross-Sectional Study

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Abstract— There are still limited data about postoperative delirium (POD) in Indonesia. The purpose of this study was to determine the prevalence of delirium in patients undergoing major orthopedic surgeries and understand its related predictors.This was a retrospective cross-sectional study done in an orthopedic hospital with medical record from January 2016 to December 2019. The subjects were over 60 years old who underwent major orthopedic surgeries (arthroplasty, internal fixation, and spine surgery). POD was diagnosed using Diagnostic and Statistical Manual of Mental Disorders (DSM-V). Univariate and Multivariate logistic regression analysis was used to analyze the possible predictors for delirium. Among 201 patients, there were 20 cases (10%) of POD. Multivariate logistic regression analysis indicated that patients with postoperative anemia [OR: 5.189 (1.086– 24.803)], given general anesthesia [OR: 9.194 (1.713 – 49.333)], limited mobility[OR: 17.575 (1.646 – 187.627)], and suffers from sleep disturbance[OR: 35.925 (8.143 – 158.497)]were more likely to develop delirium. POD's predictor seen in geriatric patients undergoing major orthopedic surgery were mobility restriction, sleep deprivation, postoperative anemia, and general anesthesia. These predictors will help to identify patients with high risk of delirium and could be a potential target for intervention.

Keywords— Postoperative Delirium, Delirium, Major Orthopedic Surgery, Geriatric, Elderly

Introduction

Postoperative delirium (POD) is a common surgical complication. It is acute, fluctuating, and can be reversed. People with high vulnerability such as geriatric population are more prone to delirium[1]. Some of the known vulnerabilities consist of older age, history of dementia, and multiple comorbidities [2]. There are many literatures writing about delirium, but the evidence is still limited in Indonesia. One study about postoperative delirium in Indonesia reported a 18.8% incidence in hospitalized elderly patients [3]. However, it is not specific for orthopedic surgeries. Geriatrics after orthopedic surgeries tend to have a higher number of POD incidences reaching 36.5% in older patient with hip fracture [4]. Even if its common, 32-67% of delirium cases were not diagnosed properly thus leading to undesirable consequences[5]. There are short- and long-term effect to POD. Short term consequences are related to symptoms of POD itself where patients become more difficult to handle. Patients with delirium could fall, remove their iv lines even catheter thus prolonging their hospitalization. While the long-term affect can end in mortality[1]. There are reports stating that 33% of POD patients could not have their cognitive function back to normal thus causing a persistent functional deficit [2]. Proper diagnosis and management could potentially reduce length of stay, additional complication, and hospital bills[1]. Therefore, this study aims to observe POD's prevalence and its predictor in geriatrics undergoing major orthopedic surgeries in one specific orthopedic specialty hospital.

Material and Methods

Study Design

This is a cross-sectional study using medical records conducted at one orthopedic hospitalfrom January 2016 to December 2019. This study was approved by theethical committee of Faculty of MedicineAirlangga University (1816/UN3.1.1/PPd.10/2019).

Assessment of Predictors

The participants were patients older than 60 years old who underwent elective major orthopedic surgery including: arthroplasty such as Total knee replacement (TKR), Total hip replacement (THR), and bipolar hemiarthroplasty; Open reduction internal fixation (ORIF); Spine surgery comprised of Interspinous fixation device (ISD), vertebroplasty, decompression and stabilization, kyphoplasty, and Percutaneous endoscopic lumbar discectomy (PELD). Patients with psychiatric medication or incomplete medical records were excluded. This study determined possible predictors which was identified as risk factors in previous literatures.Demographic information was collected during the first admission by medical personnel. Medical diagnoses, drug use, and information regarding anesthetic, and surgical procedures were collected from medical and anesthesiologic records.Comorbiditieswere measured by Charlson Comorbidity Index (CCI)[6]. Mobility restriction was evaluated preoperatively whether the patient depends on tools for reassurance or caregiver to perform daily living.Clinical laboratory data included: **(a)** Preoperative Albumin (Alb) [3.8-5.1 g/dL]; **(b)** Postoperative electrolyte: Natrium (Na) [134-145 mmol/L]; **(c)** Hemoglobin [<12 g/dL]. Pain was routinely measured beforeand after surgeryusing Numerical Rating Scale (NRS) scale pain. Sleep disturbance was registered based on the nurseor care giver's report. Opioid analgesic included were fentanyl and pethidine which was administered intravenously post-surgery according to the physician decision.Indication for postoperative ICU care are unstable hemodynamic, thoracic manipulation or performance that could affect respiratory, geriatric patient with unstable vital signs and anesthesia and/or surgery difficulties, and critical post orthopedic surgery. In order to determine the duration of surgery, it was defined the moment patient entered and exit the operating room.

Definition of Postoperative Delirium

POD was diagnosed by a neurologist using Diagnostic and Statistical Manual of Mental Disorders (DSM-V)[7]when signs and symptoms were reported by nurses or close relatives. All POD patients were treated according to the cause. Antipsychotics such as haloperidol were given to severe delirium to treat the delusions, paranoia, and perceptual disturbances.

Statistical Analysis

Data were presented with mean±standard deviation for numerical and n (%) for categorical. A bivariate analysis was performed usingChi-square or Fisher exact test for categorical variable and Mann-Whitney U test for continuous variable to compare each group. Some variables will be selected as reference to perform multivariate analysis. Univariate logistic regression will be executed first to identify correlated items and variables with $p < 0.25$ will be included inmultivariate logistic regression analysis using stepwise method.Variables are considered significant if $p < 0.05$. Data were analyzed using SPSS ver 23.00.

Results

There were total of 248 geriatric patients undergoing major orthopedic surgery from January 2016 to December 2019, and 201 patients met the inclusion criteria.Out of 201 patients, 148 (82%) were female and 88 of the patients were in the age group of 60 to 70 years old (43.8%). Patients who developed POD tend to have longer days of hospitalization (±2.1 days). In this study the CCI score started from 2, which was a minimum score since all subjects were categorized upon 60 years old and above. There was no significant

difference in NRS score in both groups. According to the hospital protocol, arthroplasty surgery is performed under regional anesthesia, which makes it usedmore frequently in both groups (149/201). Among 201 cases, POD can be found in 20 patients (10%). All of POD emerged in the ward, and no case was discovered in the recovery room, ICU or post-anesthesia period. Patients were moved to the ward after roughly 3 hours in the recovery room.The prevalence of POD varied among patients with difference surgeries: 11.19% (15/134) for arthroplasty, zero case for internal fixation and 11% (5/46) for spine surgery. The complete demographic and characteristics of the subject can be seen in **Table 1**.There wasno mortality occurred during the subject's hospitalization.

Table 1. Subject's Characteristics (N=201)

Characteristics	Delirium (N=20)	Non-Delirium (N=181)	p-value
Age	78.35 (±9.68)	72.21 (±7.73)	<0.006
Gender (F/M)	12/8	136/45	NS
BMI	23.47 (±4.49)	24.86 (±5.01)	NS
Mobility Restriction	19 (95)	99 (54.96)	<0.001
Postoperative ICU care	9 (45)	16 (8.83)	<0.000
Sleep Deprivation	16 (80)	24 (13.25)	<0.000
Opioid Analgesic	12 (60)	123 (67.95)	NS
Length of Stay (days)	8.45 (±5.34)	6.35 (±2.88)	<0.008
CCI	4.55 (±1.5)	3.28 (±1.05)	<0.000
Pre-operative NRS	4.55 (±1.39)	4.69 (±1.45)	NS
Post-operative NRS	2.7 (±0.57)	2.89 (±0.99)	NS
Type of Anesthesia			<0.010
General	7 (35)	21 (12)	
Regional	13 (65)	160 (88)	
Duration of Surgery (minutes)	168.25 (±112)	138.5 (±54.83)	NS
Preoperative Laboratory Test			
Albumin (g/dL)	2.7 (±1.39)	3.82 (±0.75)	<0.015
Hemoglobin (g/dL)	11.41 (±1.66)	12.62 (±1.45)	<0.002
Postoperative Laboratory Test			
Electrolyte Natrium (mmol/L)	136.75 (±5.34)	137.19 (±4.11)	NS
Hemoglobin (g/dL)	10.85 (±1.43)	12.01 (±1.51)	<0.001

NS= Not significant; BMI= Body Mass Index; NRS= Numerical Rating Scale; CCI=Charlson Comorbidity Index

Bivariate analysis showed that the predictors associated with POD (**Table 1**) are older age, restricted mobility preoperatively, need postoperative ICU care, sleep deprivation, longer length of stay,higher CCI, preoperative hypoalbuminemia, pre-postoperative anemia, and under general anesthesia. After performing univariate analysis, predictors with $p < 0.25$ were included in the multivariate analysis. From the multivariate logistic regression analysis, there were 4 indicative predictors for POD (**Table 2**): mobility restriction ($p = 0.018$), sleep deprivation ($p = 0.000$), postoperative anemia ($p = 0.039$), and general

anesthesia (p = 0.01).

Table 2. Univariate and Multivariate of Predictors analysis for POD

Predictors	Univariate			Multivariate		
	p-value	O.R	95% C.I.	p-value	O.R	95% C.I.
Demographic Factors						
Age						
60-70 (Ref)	-	-	-	-	-	-
71-80	0.167	2.400	(0.694 – 8.305)	0.698	-	-
80-90	0.018*	5.040	(1.318 – 19.280)	0.404	-	-
>90	0.007*	21.000	(3.232-189.851)	0.687	-	-
Gender						
Male	0.151	2.015	(0.775 – 5.241)	0.197	-	-
Female (Ref)	-	-	-	-	-	-
BMI						
<17 (Ref)	-	-	-			
17-18.4	0.906	1.200	(0.059 – 24.472)			
18.5-25	0.732	0.680	(0.075 – 6.183)			
25.1-27	0.461	0.333	(0.018 – 6.191)			
>27	0.715	0.655	(0.067 – 6.390)			
Mobility Restriction						
Yes	0.008*	15.737	(2.063 – 120.073)	0.018*	17.575	(1.646 – 187.627)
No (Ref)	-	-	-	-	-	-
Postoperative ICU care						
Yes	0.000*	8.437	(3.044 – 23.388)	0.161	-	-
No (Ref)	-	-	-	-	-	-
Sleep Deprivation						
Yes	0.000*	26.167	(8.066 – 84.889)	0.000*	35.925	(8.143 – 158.497)
No (Ref)	-	-	-	-	-	-
CCI						
2-3 (Ref)	-	-	-	-	-	-
4-5	0.025*	3.526	(1.174 – 10.590)	0.279	-	-
6-7	0.015*	10.900	(1.599 – 74.314)	0.965	-	-
>7	0.999	-	-			
Pre-operative NRS						
1-3 (Ref)	-	-	-			
4-6	0.663	0.784	(0.263 – 2.340)			
7-10	0.899	0.894	(0.157 – 5.077)			

Albumin						
<3.8	0.034*	2.954	(1.086 – 8.035)	0.926	-	-
3.8-5.1 (Ref)	-	-	-	-	-	-
>5.1	0.999	-	-			
Hemoglobin						
< 12	0.009*	3.528	(1.365 – 9.118)	0.681	-	-
≥ 13 (Ref)	-	-	-	-	-	-
Postoperative Factors						
Use of Opioid Analgesic						
Yes	0.474	0.707	(0.274 – 1.824)			
No (Ref)	-	-	-	-	-	-
Post-operative NRS						
1-3 (Ref)	-	-	-			
4-6	0.266	0.312	(0.040 – 2.430)			
7-10	1.000	-	-			
Electrolyte						
Na						
<134	0.218	1.997	(0.665 – 6.001)	0.429	-	-
134-145 (Ref)	-	-	-	-	-	-
>145	0.281	3.595	(0.350 – 36.895)			
Hemoglobin						
< 12	0.002*	7.154	(2.025 – 25.271)	0.039*	5.189	(1.086– 24.803)
≥ 13 (Ref)	-	-	-	-	-	-
Intra-Operative						
Type of Anesthesia						
General	0.007*	4.103	(1.472 – 11.438)	0.010*	9.194	(1.713 – 49.333)
Regional (Ref)	-	-	-	-	-	-
Duration of Surgery						
<60 (Ref)	-	-	-			
60-90	0.961	1.059	(0.105 – 10.680)			
91-150	0.990	0.986	(0.110 – 8.832)			
151-210	0.443	0.375	(0.031 – 4.586)			
>210	0.406	2.647	(0.267 – 26.245)			

BMI: Body Mass Index; NRS: Numerical Rating Scale; CCI: Charlson Comorbidity Index; * = significant ($p < 0.05$)

Discussion

POD is a common surgical complication. Nevertheless, it is a problem for physician because of its heterogenicity in etiology and symptoms.POD can become a serious complication if not treated properly. There are many suggestions about its risk factors, but there is not any official guideline in Indonesia that could help design an effective prevention or management approach, especially in geriatrics with major

orthopedic surgeries.This study showed that the prevalence of POD from January 2016 to December 2019 was 10%.Many studies report a similar number of POD cases in orthopedic surgeries[8–12]. Hip fractures are among the most commonly known risk factors for delirium. It occurs more frequently because of its lack of preparation in an emergency circumstances[13]. This can be seen in studies focusing on geriatric with hip fractures where the incidences of POD were over 15% [4,14–16]. In this study, patients who underwent THR were not categorized as emergency surgeries. The patients were hospitalized to prepare all of the arrangements of the surgery thus was classified as an elective surgery. On the other hand, there are also studies which found incidence rate of lower than 5% in an orthopedic environment[17–20]. There are many factors effecting this divergence. This study used DSM-V, while other research can use Confusion Assessment Method (CAM) or even other diagnostic criteria which makes the comparison not consistent [12].

The other aim of this study is to understand the possible predictors for POD after major orthopedic surgeries.Older age is one of the most associated risk factors for delirium[12,21–24], yet it is not statistically significant in this multivariate analysis. We hypothesized that an older age itself, does not always means followed by other disablements. Delirium is heavily influenced by impairment in attention, memory, and thinking which is usually found in an elderly's mind because of homeostasis change [25]. However, according to a systematic review, among 8 studies only 2 showed significant association between age and POD using a multivariate model[26]. That means, age should be assessed carefully and should not be used independently to stratify a patient's condition [27].

In this study, we found that 90% of POD patients suffered from mobility limitation before surgery. A study focusing on POD in major abdominal surgery stated that confining a patient after a surgery has a higher chance for them to develop disturbances in orientation, perception and sleep [28]. Sleep is one of the factors that we found related to POD. Sleep disturbance, especially in hospitalized patients are very common. This is an important finding because a meta-analysis stated that patients with history of sleep deprivation are 5 times more likely to develop POD rather than those who not [29]. Understanding this concern, a prospective cohort study focusing on sleep disruption stated that hospital should have created the most conducive hospital condition so patients can sleep at ease. There are also evidences stating that even before being admitted, patients already suffer from sleep disturbancethus it could persist until after the surgery [30].

Type of anesthesia is a risk factor that is still undetermined. Same with delirium incidence, high heterogenicity in each study causes different results. A systematic review reported that there was not enough evidence to suggest anesthesia type can possibly cause POD [31]. In support of this a study reported that delirium is common in both general and regional anesthetic in an orthogeriatric population [32]. We found that 65% of POD patients underwent regional anesthesia, but the higher number of regional anesthesia in both groups may cause an imbalance thus lacking normal distribution. Nevertheless, a randomized controlled trial observed a lower bi-spectral index (tool to monitor depth of anesthesia) was associated with lower case of delirium [33].

Hypoxic state like anemia is related to POD [34]. There are various factors that could affect a patient's SaO_2, thus we evaluated both pre and postoperative hemoglobin. Identical with other predictors, there are several studies reporting contrasting result. Myint et. al reported that in an acute surgical setting, there wasn't enough evidence for anemia to effect cognitive outcome [35]. While a study by Kunz et. al showed that postoperative anemia might be associated with POD [36].

In understanding these predictors, we found both modifiable and non-modifiable risk factors. Because of

delirium multiple etiologies, a proper management can be performed in various ways. In a case of elective major orthopedic surgery such as this study, it might be favorable to normalize hemoglobin level before a surgery. Proper sleep promotion and circadian intervention could be conducted to optimize the quality of sleep [37]. For limited mobility, an early ambulation training is a possibility [17]. The use of bi-spectral index (BIS) guided anesthesia to control the depth of anesthesia is also recommended. Many studies found that POD incidence was reduced after adding BIS to their protocol [33].

Even though the case of POD is now declining[17] there is still a high chance of it rising again due to increasing numbers of geriatric population. It can be predicted that almost all geriatrics will demand an arthroplasty surgery in the future [18].A proper evidence based prevention is needed to face these upcoming challenges.

This study has limitations. First, major orthopedic surgeries are based on the hospital concept of a major surgery and thus could not represent the incidence of POD across all types of orthopedic surgeries. Second, this is a retrospective cross-sectional study thus not adapting randomization.

Conclusion and Recommendation

In conclusion, this study showed that the prevalence of POD in geriatrics after a major orthopedic surgery is 10% (21/201). We found that preoperative mobility restriction, sleep deprivation, postoperative anemia, and general anesthesia were independent predictors for POD. Surgeon, neurologist, anesthetist, and all of medical personnel as a multidisciplinary team should be able to identify these predictors to prevent unwanted outcomes, especially by tending modifiable factors.

Competing Interests

The author(s) declared that there is no conflict of interest.

References

[1] Kukreja D, Günther U, Popp J. Delirium in the elderly: Current problems with increasing geriatric age. Indian J Med Res. 2015;142(6):655–62.

[2] Reddy SV, Irkal JN, Srinivasamurthy A. Postoperative delirium in elderly citizens and current practice. J Anaesthesiol Clin Pharmacol. 2017;33(3):291–9.

[3] Isfandiaty R, Harimurti K, Setiati S, Roosheroe AG. Incidence and predictors for delirium in hospitalized elderly patients: a retrospective cohort study. Acta Med Indones. 2012;44(4):290–7.

[4] Sieber FE, Neufeld KJ, Gottschalk A, Bigelow GE, Oh ES, Rosenberg PB, 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(11):987–95.

[5] Florou C, Theofilopoulos D, Tziaferi S, Chania M. Post-Operative Delirium in Elderly People Diagnostic and Management Issues of Post-Operative Delirium in Elderly People. In: GeNeDis 2016: Genetics and Neurodegeneration. 2017. p. 301–12.

[6] Chalrson ME, Pompei P, Ales KL, Mackenzie CR. a New Method of Classifying Prognostic in Longitudinal Studies : Development. J Chronic Dis. 1987;40(5):373–83.

[7] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders [Internet]. Vol. 9, Chirality. American Psychiatric Association; 2013. 395–406 p.

[8] De Santana Bosmak F, Gibim PT, Guimarães S, Ammirati AL. Incidence of delirium in postoperative patients treated with total knee and hip arthroplasty. Rev Assoc Med Bras. 2017;63(3):248–51.

[9] Jiang X, Chen D, Lou Y, Li Z. Risk factors for postoperative delirium after spine surgery in middle- and old-aged patients. Aging Clin Exp Res. 2017;29(5):1039–44.

[10] Ravi B, Pincus D, Choi S, Jenkinson R, Wasserstein DN, Redelmeier DA. Association of Duration of Surgery With Postoperative Delirium Among Patients Receiving Hip Fracture Repair. JAMA Netw open. 2019;2(2):e190111.

[11] Susano MJ, Scheetz SD, Grasfield RH, Cheung D, Xu X, Kang JD, et al. Retrospective Analysis of Perioperative Variables Associated with Postoperative Delirium and Other Adverse Outcomes in Older Patients after Spine Surgery. J Neurosurg Anesthesiol. 2019;31(4):385–91.

[12] Wang LH, Xu DJ, Wei XJ, Chang HT, Xu GH. Electrolyte disorders and aging: Risk factors for delirium in patients undergoing orthopedic surgeries. BMC Psychiatry. 2016;16(1):1–7.

[13] Bruce AJ, Ritchie CW, Blizard R, Lai R, Raven P. The incidence of delirium associated with orthopedic surgery: A meta-analytic review. Int Psychogeriatrics. 2007;19(2):197–214.

[14] Oh ES, Sieber FE, Leoutsakos JM, Inouye SK, Lee HB. Sex Differences in Hip Fracture Surgery: Preoperative Risk Factors for Delirium and Postoperative Outcomes. J Am Geriatr Soc. 2016;64(8):1616–21.

[15] Wang C guang, Qin Y fei, Wan X, Song L cheng, Li Z jun, Li H. Incidence and risk factors of postoperative delirium in the elderly patients with hip fracture. J Orthop Surg Res. 2018;13(1):1–7.

[16] Wang L, Seok S, Kim S, Kim K, Lee S, Lee K. The Risk Factors of Postoperative Delirium after Total Knee Arthroplasty. J Knee Surg. 2017;30(6):600–5.

[17] Urban MK, Sasaki M, Schmucker AM, Magid SK. Postoperative delirium after major orthopedic surgery. World J Orthop. 2020 Feb 18;11(2):90–106.

[18] Memtsoudis S, Cozowicz C, Zubizarreta N, Weinstein SM, Liu J, Kim DH, et al. Risk factors for postoperative delirium in patients undergoing lower extremity joint arthroplasty: A retrospective population-based cohort study. Reg Anesth Pain Med. 2019;44(10):934–43.

[19] Rade MC, YaDeau JT, Ford C, Reid MC. Postoperative Delirium in Elderly Patients After Elective Hip or Knee Arthroplasty Performed Under Regional Anesthesia. HSS J. 2011;7(2):151–6.

[20] Song K-J, Ko J-H, Kwon T-Y, Choi B-W. Etiology and Related Factors of Postoperative Delirium in Orthopedic Surgery. Clin Orthop Surg. 2019;11(3):297.

[21] Bin Abd Razak HR, Yung WYA. Postoperative Delirium in Patients Undergoing Total Joint

Arthroplasty: A Systematic Review. J Arthroplasty. 2015;30(8):1414–7.

[22] Elsamadicy AA, Adogwa O, Lydon E, Sergesketter A, Kaakati R, Mehta AI, et al. Depression as an independent predictor of postoperative delirium in spine deformity patients undergoing elective spine surgery. J Neurosurg Spine. 2017;27(2):209–14.

[23] Oe S, Togawa D, Yamato Y, Hasegawa T, Yoshida G, Kobayashi S, et al. Preoperative Age and Prognostic Nutritional Index Are Useful Factors for Evaluating Postoperative Delirium among Patients with Adult Spinal Deformity. Spine (Phila Pa 1976). 2019;44(7):472–8.

[24] Pinho C, Cruz S, Santos A, Abelha FJ. Postoperative delirium: age and low functional reserve as independent risk factors. J Clin Anesth. 2015;33:507–13.

[25] Ali S, Patel M, Jabeen S, Bailey RK, Patel T, Shahid M, et al. Insight into delirium. Innov Clin Neurosci. 2011;8(10):25–34.

[26] Oh ES, Li M, Fafowora TM, Inouye SK, Chen CH, Rosman LM, et al. Preoperative risk factors for postoperative delirium following hip fracture repair: A systematic review. Int J Geriatr Psychiatry. 2015;30(9):900–10.

[27] Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Audisio R, Borozdina A, et al. European Society of Anaesthesiology evidence-based and consensus-based guideline on postoperative delirium. Eur J Anaesthesiol. 2017;34(4):192–214.

[28] Brouquet A, Cudennec T, Benoist S, Moulias S, Beauchet A, Penna C, et al. Impaired mobility, ASA status and administration of tramadol are risk factors for postoperative delirium in patients aged 75 years or more after major abdominal surgery. Ann Surg. 2010;251(4):759–65.

[29] Fadayomi AB, Ibala R, Bilotta F, Westover MB, Akeju O. A Systematic Review and Meta-Analysis Examining the Impact of Sleep Disturbance on Postoperative Delirium. Crit Care Med. 2018;46(12):e1204–12.

[30] Leung JM, Sands LP, Newman S, Meckler G, Xie Y, Gay C, et al. Preoperative Sleep Disruption and Postoperative Delirium. J Clin Sleep Med. 2015;11(8):907–13.

[31] Patel V, Champaneria R, Dretzke J, Yeung J. Effect of regional versus general anaesthesia on postoperative delirium in elderly patients undergoing surgery for hip fracture: A systematic review. BMJ Open. 2018;8(12).

[32] Ilango S, Pulle RC, Bell J, Kuys SS. General versus spinal anaesthesia and postoperative delirium in an orthogeriatric population. Australas J Ageing. 2016;35(1):42–7.

[33] Janssen TL, Alberts AR, Hooft L, Mattace-Raso FUS, Mosk CA, Van Der Laan L. Prevention of postoperative delirium in elderly patients planned for elective surgery: Systematic review and meta-analysis. Clin Interv Aging. 2019;14:1095–117.

[34] Maldonado JR. Delirium pathophysiology: An updated hypothesis of the etiology of acute brain failure.

Int J Geriatr Psychiatry. 2018;33(11):1428–57.

[35] Myint PK, Owen S, McCarthy K, Pearce L, Moug SJ, Stechman MJ, et al. Is anemia associated with cognitive impairment and delirium among older acute surgical patients? Geriatr Gerontol Int. 2018;18(7):1025–30.

[36] Kunz JV, Spies CD, Bichmann A, Sieg M, Mueller A. Postoperative anaemia might be a risk factor for postoperative delirium and prolonged hospital stay: A secondary analysis of a prospective cohort study. PLoS One. 2020;15(2):1–12.

[37] Lu Y, Li YW, Wang L, Lydic R, Baghdoyan HA, Shi XY, et al. Promoting sleep and circadian health may prevent postoperative delirium: A systematic review and meta-analysis of randomized clinical trials. Sleep Med Rev [Internet]. 2019;48:101207. Available from: https://doi.org/10.1016/j.smrv.2019.08.001