

ปัจจัยทำนายภาวะสับสนเฉียบพลันหลังผ่าตัดในผู้สูงอายุที่เข้ารับการผ่าตัดใหญ่
Predictive Factors of Postoperative Delirium among Older Adults Undergoing
Major Surgery in the Eastern Region of Thailand

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บทคัดย่อ

การวิจัยเชิงทำนายนี้มีวัตถุประสงค์เพื่อศึกษาปัจจัยทำนายการเกิดภาวะสับสนเฉียบพลันในผู้สูงอายุที่ได้รับการผ่าตัดใหญ่ กลุ่มตัวอย่างคือผู้สูงอายุที่ได้รับการผ่าตัดใหญ่ มีคุณสมบัติตามเกณฑ์ที่กำหนด จำนวน 132 คน คัดเลือกด้วยการสุ่มอย่างง่าย เก็บรวบรวมข้อมูลโดยวิธีการสัมภาษณ์ เครื่องมือที่ใช้ในการวิจัยครั้งนี้ประกอบด้วย แบบบันทึกข้อมูลส่วนบุคคล แบบวัดความเครียดในผู้สูงอายุฉบับภาษาไทย แบบประเมินความวิตกกังวลขณะเผชิญ แบบประเมินความปวด และแบบประเมินภาวะสับสนเฉียบพลันฉบับภาษาไทย วิเคราะห์ข้อมูลด้วยสถิติพรรณนาและการวิเคราะห์ถดถอยเชิงเส้นพหุคูณแบบขั้นตอน

ผลการวิจัยพบว่าผู้สูงอายุกลุ่มตัวอย่างมีภาวะสับสนเฉียบพลันหลังผ่าตัดใหญ่ร้อยละ 22.70 ปัจจัยที่สามารถทำนายการเกิดภาวะสับสนในผู้สูงอายุที่เข้ารับการผ่าตัดใหญ่ได้สูงสุดคือ ภาวะซึมเศร้า ($\beta = .452$, $p < .001$) รองลงมาคือ อายุ ($\beta = .290$, $p < .001$) จำนวนชนิดยา ($\beta = .258$, $p < .001$) และความปวดหลังผ่าตัด ($\beta = .172$, $p < .001$) ตามลำดับ โดยร่วมทำนายการเกิดภาวะสับสนในผู้สูงอายุที่เข้ารับการผ่าตัดใหญ่ได้ถึงร้อยละ 64.7 ($R^2 = .647$ $p < .001$)

ผลการวิจัยแสดงให้เห็นว่าภาวะซึมเศร้า อายุ จำนวนชนิดยา และความปวดหลังผ่าตัด เป็นตัวแปรที่มีอิทธิพลต่อการเกิดภาวะสับสนเฉียบพลันหลังผ่าตัดใหญ่ในผู้สูงอายุ ดังนั้นพยาบาลและบุคลากรทางสุขภาพที่เกี่ยวข้องควรให้ความสำคัญกับผลกระทบของปัจจัยดังกล่าวต่อการเกิดภาวะสับสนเฉียบพลันหลังผ่าตัดใหญ่ในผู้สูงอายุ และนำมาใช้ในการพัฒนารูปแบบการป้องกันสุขภาพผู้สูงอายุที่เข้ารับการผ่าตัดใหญ่เพื่อลดการเกิดภาวะสับสนเฉียบพลันหลังผ่าตัดใหญ่ต่อไป

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คำสำคัญ: ภาวะสับสนเฉียบพลันหลังผ่าตัด, การผ่าตัดใหญ่, ภาวะซึมเศร้า, ความเจ็บปวด, ผู้สูงอายุ

ABSTRACT

This predictive research aimed to examine predictive factors of delirium among older adults undergoing major surgery. A simple random sampling technique was used to recruit 132 older adults undergoing major surgery, who met the inclusion criteria. Depression, perioperative anxiety, and delirium were assessed by the Thai Geriatric Depression Scale: Short Version (TGD-15), the State-Trait Anxiety Inventory Form Y-1 (STAI Form Y-1), and the Thai Delirium Rating Scale (TDRS), which demonstrated Cronbach's alpha coefficients of .87, .86, and .93, respectively. Pain Numeric Rating Scale (NRS) was used for measuring pain intensity, with a test-retest reliability of .94. Data were analyzed using descriptive statistics, and stepwise multiple regression.

The research findings revealed that 22.70% of the older adults experienced postoperative delirium. Factors with the highest predictive power for postoperative delirium were depression ($\beta = .452, p \leq 0.001$), followed by age ($\beta = .290, p \leq .001$), number of medications ($\beta = .258, p \leq .001$), and postoperative pain ($\beta = .172, p \leq .001$) respectively. These four factors explained 64.7% of the variance for postoperative delirium ($R^2 = .647, p \leq .001$). Thus, nurses and health care providers should consider the effects of these contributing factors on postoperative delirium among older adults undergoing major surgery and devise a program to prevent and alleviate postoperative delirium in older adults undergoing major surgery.

Keywords: Postoperative delirium, Major surgery, Depression, Pain, Older adult

Introduction

Delirium is common among hospitalized elderly patients, with its incidence and prevalence varying significantly. Approximately 15% to 30% of elderly patients exhibit delirium upon hospital admission, and up to 56% may develop it during their stay (Lamaroon et al., 2020). Postoperative delirium (POD) is a frequent complication in this population, characterized by acute cognitive and intentional dysfunction following major surgery. The incidence of POD varies widely depending on the patient population, with rates as high as 87%, influenced by patient age and the type of surgery performed (Kang et al., 2020).

POD occurs more frequently after major surgery including orthopedic surgeries, abdominal surgery, vascular surgery and spinal surgeries (Gao, Ma, Li, Yin, & Li, 2020; Gutierrez et al., 2024; Heo, Ahn, Shin, Lim, & Han, 2020; Sui, Duan, Liu, & Li, 2021). The development of POD is influenced by multiple factors, with known risk factors present at each stage of operative care. Age is a significant risk factor, with patients over 70 years old being at a higher risk for POD (An et al., 2023). Preoperative risk factors include comorbidities, malnutrition, preexisting cognitive impairments, impaired physical functional status, preexisting depression and anxiety, anemia and poly pharmacy (Jin, Hu & Ma, 2020; Kang et al., 2020; Katlic & Robinson, 2021). Intraoperative risk factors include prolonged operative time (Ravi et al., 2019), general anesthesia (Bocskai et al., 2020), required blood transfusions, and the type of surgery. Postoperatively, uncontrolled pain and high doses of opioids also increase the incidence of POD (Samuel et al., 2022). As the population ages, an increasing number of older adults are undergoing major surgeries (Becher, Lund, Coats, & Savarese, 2022). POD is linked to several adverse outcomes, including prolonged mechanical ventilation and extended ICU stays (Lat et al., 2009), longer hospitalizations, higher risk of readmission, impaired physical functioning, and increased mortality rates by at least 10–20% for every 48 hours of delirium (Samuel et al., 2022; Shehabi et al., 2019). A meta-analysis has shown that experiencing delirium during hospitalization doubles the risk of post-discharge institutionalization and death, as well as increases the likelihood of developing dementia

(Gerakios et al., 2024). Furthermore, delirium has significant implications for both patients and healthcare systems. A recent study in the US found that delirium in older adults undergoing major elective surgery is estimated to increase healthcare costs by US\$44,291 per patient over one year (Gou et al., 2021).

Although there are numerous studies on the risk factors for postoperative delirium in elderly patients undergoing major surgery, most of these studies have been conducted in Western contexts. Research on postoperative delirium among older adults undergoing major surgery in Thailand is limited, and studies specifically from the Eastern Region of Thailand are nonexistent. Additionally, existing research on postoperative delirium in older adults undergoing major surgery often does not address the predisposing and precipitating factors based on the multifactorial model of delirium in older persons (Inouye, Westendorp & Saczynski, 2014). Therefore, the study identifying predictors of postoperative delirium among older adults undergoing major surgery in Thailand is needed. Routine assessment of postoperative delirium among older adults undergoing major surgery could facilitate the results of this study because multiple factors that considered as risk factor of delirium might be interdependent with postoperative delirium among older adults undergoing major surgery. The purpose of this study is to examine relationships between the set of predictors and postoperative delirium among older adults undergoing major surgery.

Conceptual framework

In this study, the researchers utilized the multifactorial models of delirium proposed by Inouye et al. (2014) alongside a comprehensive literature review as a conceptual framework. According to Inouye et al. (2014), delirium in the elderly is driven by multiple factors. These include predisposing factors existing characteristics in the elderly prior to surgery and precipitating factors new conditions that trigger acute confusion post-surgery. The researchers identified age, the number of medication types, preoperative anxiety, and depression as predisposing factors, while postoperative pain was recognized as a precipitating factor. These elements are closely linked to the development of delirium in older adult patients undergoing major surgery as presented in the Figure 1

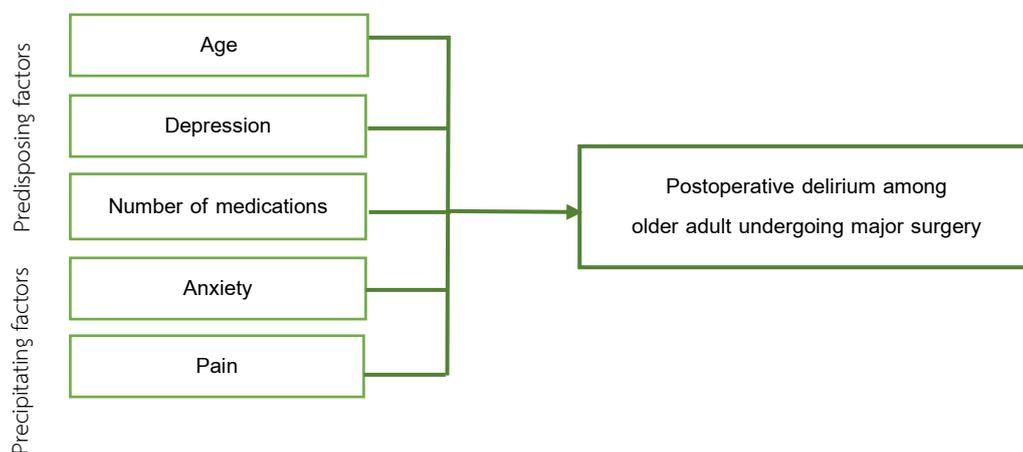


Figure 1 Conceptual framework

Method

Design and Sample

This descriptive study was conducted among elderly patients undergoing major surgery in the Eastern Region of Thailand. Simple random sampling was used to select the participants admitted to one of six general hospitals in the Eastern Region of Thailand. The sample size was calculated using G-power analysis software. Based on multiple regression statistics, the parameters were estimated as follows: Tail = two, effect size = .10, α err prob = .05, Power ($1-\beta$ err prob) = .95. A total sample size of 132 was calculated. The inclusion criteria were: (1) aged ≥ 60 years old both male and female, (2) admitted to the hospital as an elective case of major surgery with general anesthesia, (3) no cognitive impairment based on MMSE-Thai screening tool, (4) no alcohol independence syndrome based on ICD 10 identification, (5) can communicate and understand Thai language, and (6) willing to participate in this study. An exclusion criterion was the elderly patients undergoing major surgery and having plans to stay in an intensive unit after major surgery.

Measures

Permission to use each instrument was obtained from the original authors before data collection. The participants were screened for cognitive impairment using the MMSE-Thai (Folstein, Folstein & McHugh, 1975). The questionnaire is composed of 5 parts. The description of the 5 questionnaires is as follows. 1) The demographic questionnaire collected

data on age, gender, religion, marital status, occupational, education level, income, current illnesses, number of medications use, and drinking alcohol history. 2) The Thai Geriatric Depression Scale: Short Version (TGD-15) was used to measure depression. The TGDS-15 is a self-administered assessment that focuses on psychiatric symptoms such as mood (e.g., emptiness, boredom, and life satisfaction) and cognitive changes rather than somatic symptoms (e.g., weight loss and sleep disturbances). The TGDS-15 has demonstrated good internal consistency among the older Thai population (Tangthong & Manomaipiboon, 2023). It comprises 15 questions, with yes and no scored as 1 and 0, respectively, and a maximum score of 15 points. A total score ≥ 5 was classified as the cutoff to detect significant depression symptoms (Wongpakaran, Wongpakaran, & Van Reekum, 2013) and Cronbach's alpha coefficient was .87. 3) The State-Trait Anxiety Inventory Form Y-1 (STAI Form Y-1) was used to assess anxiety of the participants. The STAI-Y is a self-report questionnaire consisting of two 20-item scales providing separate measures of state and trait anxiety (S-Anxiety and T-Anxiety, respectively). This study used only a State-Anxiety. S-Anxiety is a transitory response to an event perceived as adverse, characterized by feelings of tension, apprehension, nervousness, and worry. The S-Anxiety scale includes twenty items evaluating how the subject feels "right now, at this moment". On a 4-point Likert scale (1–4), a score equal to 4 indicates the presence of a higher level of anxiety. The total score ranges from 20 to 80, with higher scores indicating more severe anxiety (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) and Cronbach's alpha coefficient was .86. 4) Pain Numeric Rating Scale (NRS) was used for measuring pain intensity. The NRS is commonly used for measuring pain intensity and is well validated. It is scored from 0–10 (0 meaning no pain and 10 meaning the worst pain imaginable) Participants are instructed to choose a single number from the scale that best indicates their level of pain (Nugent, Lovejoy, Shull, Dobscha, & Morasco, 2021) and 5) The Thai Delirium Rating Scale (TDRS) was used to measure delirium. The scale was initially developed by Zartrungpak, Prasertchai, Jennawasin, and Saipanish (2001) and consists of 6 items with overall scores ranging from 0-20. A total score ≥ 10 was classified as the cutoff to detect significant delirium and Cronbach's alpha coefficient was .93.

Ethical Considerations

The letter of approval was obtained from Research Ethics Committee of Burapha University (IRB3 053/2563) and Chon Buri Hospital (No 085/2565). Written consent was obtained from the elderly patients for participation in the study. Patients' names were not included in the data collection forms to ensure confidentiality

Data Collection Process

The data collection took place between December 2022 to April 2023. The MMSE instrument, which takes 5-10 min to complete, was used to screen the elderly patient undergoing major surgery willing to participate in the study. A total of 132 elderly patients who met the inclusion criteria were selected. After obtaining informed consent, personal data, depression, anxiety, the researchers collected the number of medications through a face-to-face interview on the first day of hospital admission. Pain score and delirium were assessed on the third day post-major surgery, taking approximately 20-30 minutes. The questionnaires were checked for completeness and numbered at the end of data collection. All the data were kept confidential, and only the researchers had access to the data.

Data Analysis Process

A statistical software program was utilized to analyze the data. Descriptive statistics were employed to summarize the demographic characteristics of the participants, while Pearson's correlation was used to examine the relationships among the variables. Stepwise multiple linear regression was conducted to identify the predictive factors of postoperative delirium. For all tests in this study, a p-value of less than 0.05 was considered statistically significant.

Result

Characteristics of the Participants

The mean age of the 132 participants in this study was 69.58 years \pm 6.94) and ranged from 60 to 99 years. Most of the sample was female (54.55%). 100% of the participants were Buddhist. Most of the participants were married (81.82 %), had an income lower than 10,000 baths (59.10%), not working (43.2%), reported having had four years of primary school

education (62.10%), and no drinking alcohol (80.30%). More than half (68.90%) of the participants reported at least one chronic illness and using medication. The average scores of medications taken by these participants were 3.6 ± 3.29 (Table 1).

Table 1 Demographic Characteristics of Older Adults Undergoing Major Surgery (n=132)

Demographic Characteristic	Mean (SD)	n (%)
Age (years) (Min = 60, Max = 90)	69.58 (SD = 6.94)	
Gender		
Female		72 (54.55)
Male		60 (45.45)
Buddhist Religion		132 (100)
Marital Status		
Married		108 (81.82)
Widowed		18 (13.64)
Single		6 (4.54)
Income (Baht per month) (Min = 600, Max =40,000)	10,471.97 (10,679.69)	
< 10,000		78 (59.10)
10,001-20,000		35 (26.50)
>20,000		19 (14.40)
Occupation		
Not working		72 (54.55)
Own Business		16 (12.12)
Self-Employment		35 (26.51)
Agriculture		9 (6.82)
Educational Level		
No school		18 (13.60)
Primary school		82 (62.10)
Secondary school		16 (12.10)
Bachelor's Degree		16 (12.10)
Number of Medications (Min = 0, Max = 15)	3.16 (SD = 3.30)	6.67 (SD = 3.28)

The majority of the participants revealed had no delirium (77.30%), no depression (84.80%), mild anxiety (77.30%), and moderate pain level (72.73%) (Table 2).

Table 2 Characteristics of the Study Variables

Variable	Possible range	Actual range	Mean	SD	N (%)	Meaning
Delirium			2.59	4.74		No Delirium
	0-9				102 (77.30)	No Delirium
	10-20				30 (22.70)	Has Delirium
Depression			1.39	2.07		No Depression
	0-4				112 (84.80)	No Depression
	5-10				20 (15.20)	Has Depression
Preoperative Anxiety			33.95	6.57		Mild Anxiety
	20-40				102 (77.30)	Mild Anxiety
	41-60				30 (22.70)	Moderate Anxiety
Postoperative Pain			4.95	1.51		Moderate Pain
	1-3				30 (22.73)	Mild Pain
	4-7				96 (72.73)	Moderate Pain
	8-10				6 (4.54)	Severe Pain

Factors associated with postoperative delirium findings showed that depression, number of medications, age, postoperative pain, and preoperative anxiety were positively related to delirium ($r = .635, p < .01$; $r = .597, p < .01$; $r = .538, p < .01$; $r = .291, p < .01$; $r = .219, p < .01$, respectively) (Table 3).

Table 3 Correlation among the variables

Factors	1	2	3	4	5	6
Postoperative Delirium	1					
Depression	.635 ^{**}	1				
Number of medications	.597 ^{**}	.407 ^{**}	1			
Age	.538 ^{**}	.252 ^{**}	.408 ^{**}	1		
Postoperative pain	.291 ^{**}	.031	.216 [*]	.170	1	
Preoperative anxiety	.219 ^{**}	.324 ^{**}	.122	.237 ^{**}	.204 [*]	1

^{**} $p < .01$

^{*} $p < .05$

Predictive factors on postoperative delirium are displayed in Table 5, in the first step, depression ($\beta = .635$, $p < .01$) was the significant predictor of postoperative delirium, and accounted for 40.3 % of the variance. In the second step, depression ($\beta = .533$, $p < .01$) and age ($\beta = .404$, $p < .01$) both were significant predictors of postoperative delirium, and accounted for 55.6 % of the variance. In the third step, depression ($\beta = .438$, $p < .01$), age ($\beta = .308$, $p < .01$), and number of medications ($\beta = .293$, $p < .05$), accounted for 61.9 % of the variance. In the fourth step, depression ($\beta = .452$, $p < .01$), age ($\beta = .290$, $p < .01$), number of medications ($\beta = .258$, $p < .05$), and postoperative pain ($\beta = .172$, $p < .05$) were the significant predictors of postoperative delirium, accounted for 64.7 % of the variance (Table4)

Table 4 Predictive Factors for Postoperative Delirium

Predictive Factors	β	R	R ²	Adjust R ²	t value
Step 1		.635	.403	.399	
Depression	.635				9.371**
Step 2		.746	.556	.549	
Depression	.533				8.796**
Age	.404				6.667**
Step 3		.787	.619	.610	
Depression	.438				7.300**
Age	.308				5.136**
Number of medications	.293				4.608*
Step 4		.804	.647	.636	
Depression	.452				7.764**
Age	.290				4.973**
Number of medications	.258				4.127*
Postoperative pain	.172				3.158*

β values are standardized regression coefficients from the final stage of regression analysis.

R² values are cumulative, with each incremental step adding to the variance explained.

** $p < .01$, * $p < .05$

Discussion

Varying incidences of POD have been reported in different studies. Previous reviews noted that the incidence of delirium ranges from 14.7- 40.5% in major surgical population (Ahn & Bang, 2022; Alvarez-Bastidas, Morales-Vera, Valle-Leal & Marroquín-González, 2018; Watt et al., 2018). The risk factors included older age, anxiety, preoperative depression, number of medication use, and postoperative pain.

The incidence of POD was 22.70% in this study, which is similar to previous studies that investigated 132 older adults (60 males and 72 females; average age of 60.98± 6.94 years) undergoing major surgery. The elderly with delirium undergoing major surgery had a mean age of 76.43 ±5.73, most of them were 70–79 years old (70.00%), more than half were female (56.70%), most of them had POD within 24 hours (83.33%), almost all of them had

underlying diseases and took regular medication before surgery, all of them received general anesthesia (100%), half of them were depressed (50%), and almost all of them had moderate or higher postoperative pain. (93.33%). The findings are consistent with previous studies that found that more than half (56 -63.0%) of the participants experienced POD in the first 24 hours (Iamaroon et al., 2020; Siripoonyothai & Sindhvananda, 2021). The observed prevalence of delirium within 24 hours post-surgery underscores the immediate impact of surgical stress and anesthesia on the elderly's cognitive functions. The linkage between delirium and the inflammatory response to surgery, as evidenced by the release of proinflammatory cytokines, is consistent with findings from Kobayashi et al. (2017), highlighting the neuroinflammatory pathway's role in postoperative cognitive dysfunction.

Moreover, the study corroborates the association between multiple comorbidities, polypharmacy, and the risk of POD, with a notable percentage of patients having preexisting conditions and regular medication use (Wu, Sun & Tan, 2019). The complexity of managing multiple drugs, especially those affecting neurotransmitters, can exacerbate delirium risk, emphasizing the need for meticulous medication management in this population (Jin et al., 2020; Maldonado, 2017). Additionally, the correlation between elder age and increased delirium risk observed in this study is supported by existing research, suggesting that physiological and neurochemical changes associated with aging may contribute significantly to the vulnerability to delirium (Bilge, Kaya, Şenel & Ünver, 2015; Wu et al., 2019).

The predictive factors for POD identified depression, age, number of medications, and postoperative pain highlight critical areas for intervention to mitigate delirium risk.

Depression's role as a significant predictor aligns with the biochemical theory of depression, which postulates that neurotransmitter imbalances can influence cognitive function and, consequently, delirium risk (Fineberg et al., 2013; Inouye et al., 2015; Kazmierski et al., 2010).

The findings of this study are consistent with the previous studies. They found that depression was a predictor of POD in older adults undergoing hip fracture surgery and spinal surgery (OR = 2.02; 95% CI 1.00, 4.06; p=.049) (Ahn & Bang, 2022; Xiao, Zhang, Fang, & Yuhang, 2020).

Age is a significant predictor for postoperative delirium (POD) because older adults are more vulnerable to various physiological and cognitive changes. Aging changes contribute to postoperative delirium (POD) due to a variety of physiological and cognitive alterations that increase vulnerability in older adults. These changes include 1) Cognitive Function Decline: Older adults may have pre-existing conditions such as dementia or mild cognitive impairment, predisposing them to delirium after surgery 2) Reduced Physiological Reserve: Older adults have a diminished ability to cope with the stress of surgery and anesthesia, leading to complications such as delirium 3) Comorbidities: Advancing age increases the likelihood of having multiple chronic health conditions. These conditions can complicate the perioperative course and contribute to the onset of delirium 4) Sensory Impairments: Older adults often experience sensory impairments (such as vision or hearing loss), exacerbating confusion and disorientation in the postoperative environment, contributing to delirium (Inouye et al., 2014) and 5) Polypharmacy: Older adults are more likely to be on multiple medications, increasing the risk of drug interactions and adverse effects, including delirium. The findings of this study are consistent with the previous study. The systematical study found that POD was associated with increasing age by 1.07 times (OR 1.07; 95%CI 1.04–1.09), with those aged 65 years and older having a 4.77 -fold (OR 4.77; 95% CI 4.37–5.16) increase risk of POD, and those aged 70 years and older having a 15.87 -fold (OR 15.87; 95% CI 6.03–41.73) increase risk of POD (Wu et al., 2019) and consistent with the retrospectively studied in Korea by Ahn and Bang (2022), it was found that the elderly aged 85 years and older were 4.7 times more likely to develop POD (OR = 4.7; 95% CI 4.15-5.37).

The number of medications used is also a strong predictor of POD among respondents. Many studies corroborate our findings. For instance, research involving a Japanese cohort undergoing surgery for lung and esophageal cancer found that benzodiazepine use was a notable risk factor for POD (OR 4.0, 95% CI 1.1-14.5) (Murakawa et al., 2015). Another study also highlighted a significant link between polypharmacy and POD. They found that the use of more than six types of drugs was associated with a 3.02-fold increased risk of developing POD (OR = 3.02; 95% CI 1.39–6.81, $p = .0062$) (Kurusu, Miyabe, Furukawa, Shibayama & Yoshiuchi, 2020). This research results can explain that older adults

are often on multiple medications due to multiple health conditions. Their altered drug metabolism and clearance due to aging can lead to higher levels of medications in the system, increasing the risk of delirium. In addition, the more medications older people take, the higher the chance of drug-drug interactions. These interactions can alter the pharmacokinetics and pharmacodynamics of the drugs, leading to side effects or toxicities that may affect cognitive function. Additionally, many medications, especially those affecting the central nervous system (CNS) like benzodiazepines, opioids, and anticholinergics, can contribute to cognitive impairment and delirium. Polypharmacy increases the risk of these drugs causing adverse CNS effects (Gronich, 2024). More than that, older adults may be more sensitive to the effects of certain medications due to age-related changes in drug absorption, distribution, metabolism, and excretion. This increased sensitivity can lead to a higher risk of adverse effects, including delirium.

Postoperative pain was found to predict the occurrence of POD in older adult patients undergoing major surgery ($\beta = .172, p < .001$). The research results suggest that major surgery induces tissue and nerve damage, which triggers an inflammatory response in the body. This response involves the secretion of proinflammatory cytokines such as Interleukin-1 and tumor necrosis factor-alpha. These cytokines can cross the Blood-Brain Barrier and stimulate the brain to produce inflammatory cytokines, leading to inflammation of brain tissue. Additionally, red blood cells and fibrin can obstruct small blood vessels, reduce cerebral blood flow, and cause blood vessel constriction. This process also stimulates the sympathetic nervous system and releases abnormal neurotransmitters, contributing to the development of POD after major surgery (Kobayashi et al., 2017).

In addition, surgery introduces a mechanical stimulus that directly damages tissues and nerves, leading to the release of pain-inducing substances like Prostaglandin E2 and Substance P. These substances activate nociceptors, which transmit pain signals via A-delta and C-fibers to the spinal cord. The signals are then processed through the spinothalamic and spinoreticular tracts, reaching the cerebral cortex, hypothalamus, and limbic system—regions involved in processing fear and stress. Activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis increases systemic tone and elevates levels of catecholamines and other

hormones. In elderly patients, who may struggle with pain management, these physiological responses can disrupt rest and sleep cycles, potentially leading to POD (Inouye, 2006; Tejangkura, 2007; Thepsoparn, 2020). Major surgery leads to severe damage, bruising, and injury to tissues and nerves, resulting in acute postoperative pain. Specifically, during the first 24 hours after surgery, most participants (80.00%) experienced moderate levels of postoperative pain. Furthermore, all participants (100%) who reported severe pain had difficulty sleeping.

The findings of this study are consistent with those of Wu et al. (2019), who investigated the incidence and risk factors of postoperative delirium (POD) in patients undergoing spinal surgery. Their study found a significant association between pain levels and the occurrence of POD (OR = 1.88; 95% CI 1.11–2.64). Additionally, these results align with the study by Swart, van der Zanden, Spies, de Rooij, and van Munster (2017), which demonstrated that high levels of postoperative pain and high doses of opioids increase the risk of POD.

In this study, although the preoperative anxiety showed a positive correlation with postoperative delirium (POD), it could not predict the occurrence of POD in older adults undergoing major surgery. Despite the anxiety linked to life-threatening surgical situations, patients received comprehensive care and preparation from professional teams before their surgeries. The patients would be informed of the type of surgery, reasons for the surgery, benefits, and potential complications on the day of the surgical appointment. In addition, on the day before surgery, patients were assessed a preoperative evaluation at the inpatient ward, reinforcing both physical and mental preparation. They received information emphasizing pre-post-operative procedures and methods of administering anesthesia during the surgery. Consequently, most patients reported that their anxiety levels had reduced, perceiving the surgery as a necessary step toward recovery and a return to their normal lives. They felt hopeful that the operative procedure would enhance their quality of life, and they expressed confidence in the capabilities of the surgical team, which was equipped with specialized surgeons and advanced medical technology, including life-saving tools. Therefore, preoperative physical and mental assessment and preparation are strategies that

allow patients to adjust to maintain mental balance, affecting the level of preoperative anxiety. The study found that the majority of the elderly participants had a low level of preoperative anxiety (77.30%), so preoperative anxiety did not affect the occurrence of postoperative delirium.

These findings were consistent with the previous research by Milisen et al. (2020), which examined preoperative anxiety and POD in 190 elderly patients over 65 undergoing heart surgery, concluding that preoperative anxiety was not a predictor of POD. Similarly, Van Grootven et al. (2015) investigated risk factors for POD in elderly patients undergoing hip fracture surgery and found that preoperative anxiety did not predict POD occurrence (OR 1.18, 95% CI .89-1.56, $p = .250$).

Conclusion

This study highlights the multifaceted risk factors for postoperative delirium (POD) in older adult patients undergoing major surgery, revealing a notable incidence of delirium strongly correlated with depression, age, polypharmacy, and postoperative pain. The findings underscore the need for a holistic approach in managing older surgical patients, which should include mental health evaluations, medication management, and effective pain control to mitigate the risk of POD. Future studies could focus on preventive interventions, such as preoperative preparation training, mental health counseling, and medication reviews, to minimize the likelihood of POD and improve recovery. The insights from this study are increasingly relevant and provide a foundation for enhancing perioperative care protocols to reduce the burden of POD in the older adults undergoing major surgery.

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