BMC Geriatrics

RESEARCH

Open Access

Long-term mortality impact of postoperative hyperactive delirium in older hip fracture surgery patients

Mingyang Sun[1], Wan-Ming Chen[2,3], Szu-Yuan Wu[2,3,4,5,6,7,8,9,10,11,12*†] and Jiaqiang Zhang[1,13*†]

Abstract

Background Postoperative hyperactive delirium is a common and serious complication in older patients undergoing surgery, but the association between delirium and mortality remains controversial. Compared to other delirium subtypes, hyperactive delirium is characterized by more overt clinical manifestations, facilitating accurate detection and evaluation. This study aimed to clarify this association by comparing long-term mortality between patients with and without postoperative hyperactive delirium, using propensity score matching for robust analysis.

Methods We conducted a cohort study to evaluate the association between postoperative hyperactive delirium and long-term mortality in older patients undergoing emergency hip fracture surgery. We used the Taiwan National Health Insurance Service database to identify patients aged 65 years or older who underwent emergency hip fracture surgery between 2008 and 2018. The primary outcome was all-cause mortality.

Results A total of 270,437 patients were included in the analysis, with 6,795 patients in the postoperative hyperactive delirium group and 263,642 patients in the no postoperative hyperactive delirium group. After PSM, both groups contained 6,795 patients, ensuring balanced baseline characteristics for comparison. Postoperative hyperactive delirium was an independent risk factor for all-cause death, with an adjusted hazard ratio of 1.62 (95% confidence interval, 1.51–1.74; $P < 0.0001$) after PSM. Subgroup analysis revealed that older patients with postoperative hyperactive delirium consistently exhibited significantly higher adjusted hazard ratios of all-cause death compared with those without postoperative hyperactive delirium, regardless of age, sex, income levels, or ASA scores. Although the difference in 5-year overall survival between groups (81.7% vs. 89.8%, $P < 0.0001$) was statistically significant, the high survival rates in both groups suggest a modest absolute clinical impact.

Conclusion Postoperative hyperactive delirium is an independent risk factor for long-term mortality in older patients undergoing emergency hip fracture surgery. While the statistical association is evident, it is important to carefully consider the modest absolute difference in survival rates and its implications for clinical application.

†Szu-Yuan Wu and Jiaqiang Zhang contributed equally to this study (joint Correspondence authors).

*Correspondence:
Szu-Yuan Wu
szuyuanwu5399@gmail.com
Jiaqiang Zhang
zhangjiq@zzu.edu.cn

Full list of author information is available at the end of the article

Key points

- Postoperative hyperactive delirium is independently associated with an increased risk of all-cause death in older patients undergoing hip fracture surgery.
- Patients with postoperative hyperactive delirium have a significantly higher adjusted hazard ratio for all-cause death compared to those without.
- Preventing and effectively managing postoperative hyperactive delirium in this population is crucial for improving long-term outcomes and reducing mortality.

Keywords Postoperative hyperactive delirium, Mortality, Older, Hip fracture, Propensity score matching

Why does this paper matter?

This study sheds light on a critical aspect of care for older patients undergoing emergency hip fracture surgery by examining the association between postoperative hyperactive delirium and long-term mortality. The findings underscore the importance of vigilance in identifying and addressing this complication, as it significantly impacts patient outcomes. With a higher risk of all-cause death among those experiencing postoperative hyperactive delirium, the study emphasizes the urgency of implementing strategies aimed at prevention and management. By doing so, healthcare providers can potentially enhance the quality of care and prognosis for this vulnerable population. Furthermore, the study underscores the need for comprehensive approaches that encompass early detection, prevention, and tailored interventions to mitigate the adverse effects of postoperative hyperactive delirium. Ultimately, addressing this issue not only holds potential to improve individual patient outcomes but also contributes to advancing the overall standard of care for older surgical patients, thereby making a meaningful impact on healthcare practices and policies.

Introduction

Postoperative hyperactive delirium is an important issue because it is a common complication in older patients undergoing surgery [1–5], particularly those with pre-existing cognitive impairment or dementia [2–5]. Delirium can result in a range of negative outcomes, including increased morbidity, prolonged hospital stay, and increased healthcare costs. It can also have a significant impact on the patient's quality of life and functional outcomes after discharge [6–14]. Moreover, postoperative hyperactive delirium is an under-recognized and under-diagnosed problem, and its occurrence is often not documented in medical records [6]. This can lead to inadequate postoperative care and a failure to address underlying risk factors. Improved recognition and management of postoperative hyperactive delirium is needed to reduce the incidence of this condition and improve outcomes for older surgical patients [1, 14–17].

Hyperactive delirium was selected as the focus of previous studies due to its pronounced clinical features, such as agitation and restlessness, which facilitate accurate detection, assessment, and documentation compared to other delirium subtypes [18, 19]. In contrast, hypoactive delirium often presents with subtle symptoms like lethargy and reduced responsiveness, leading to frequent underdiagnosis and misclassification without the use of specific diagnostic tools [20–22]. As a result, hypoactive delirium is more challenging to study reliably in large databases [20–22]. By focusing on hyperactive delirium, prior studies aim to enhance diagnostic precision and provide robust evidence on its association with long-term outcomes [18, 19].

Several risk factors have been identified for postoperative hyperactive delirium, including age, pre-existing cognitive impairment, dementia, alcohol use, malnutrition, and multiple comorbidities [7, 23, 24]. Other risk factors include the use of general anesthesia, or prolonged duration of anesthesia [25, 26]. Environmental factors such as sleep disorder, immobility, and sensory deprivation may also increase the risk of postoperative hyperactive delirium [27, 28]. Additionally, the association between postoperative hyperactive delirium and mortality is a crucial area of research, as several studies have suggested a link between the two [29–34]. However, the relationship is controversial and is challenging to establish due to the high risk of confounding bias [9, 35–40]. Many of the risk factors for postoperative hyperactive delirium are also independent risk factors for mortality, including advanced age, comorbidity, preexisting cognitive dysfunction, and high-risk surgery [7, 23, 24]. Despite the growing body of evidence, previous reports were limited by small sample size, wide range on enrolled patients' age inhomogeneous surgical types, and a focus on short-term mortality [9, 35–40].

To address these limitations, there is a need for high-quality observational studies that consider confounding factors such as pre-existing cognitive function, dementia, and comorbidities through propensity scores matching (PSM) long-term large sample size cohort. The previous low-quality studies produced conflicting conclusions about the association between postoperative hyperactive delirium and mortality [37–39], highlighting the need for robust research. The current study aims to bridge this gap by evaluating the long-term impact of postoperative

hyperactive delirium on survival in older patients undergoing emergency hip fracture surgery, leveraging a nationwide database for comprehensive analysis.

Patients and methods

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) of Tzu-Chi Medical Foundation (Approval Number: IRB109-015-B). Given that the study utilized a de-identified dataset from the Taiwan National Health Insurance Research Database (NHIRD), informed consent was waived, as all personal identifiers had been removed before data access. The use of these datasets is regulated by Taiwan's Personal Information Protection Act, which imposes strict guidelines to ensure data security and confidentiality.

All research procedures adhered to the principles of the Declaration of Helsinki for ethical research involving human data. The study protocol was reviewed to ensure compliance with ethical guidelines, and no interventions or direct interactions with patients were involved.

Study population

This study draws on the Taiwan National Health Insurance (NHI) Research Database (NHIRD) from January 2008 to December 2018, with follow-up until December 31, 2020. The NHIRD comprises registration files and original claims data for all NHI beneficiaries, encompassing a total of approximately 27.38 million individuals. The database provides detailed information on outpatient and inpatient claims, including patient identification numbers, birth dates, sex, surgical procedures, dates of anesthesia, diagnostic codes based on the International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification (ICD-9-CM and ICD-10-CM), treatment information, medical costs, dates of hospital admission and discharge, cause of death, and date of death, all of which were collected from encrypted NHIRD data [41–47]. To link all data sets, patient identification numbers were used.

Inclusion and exclusion criteria

Our study included older patients who were 65 years or older and underwent emergency hip fracture surgery that required anesthesia in Taiwan between 2008 and 2018. Emergency hip fracture surgery is considered high-risk, especially in elderly patients, due to advanced age, comorbidities, and reduced physiological reserves [43, 48, 49]. This type of surgery is associated with significant surgical stress and a high risk of postoperative complications, including infections, cardiovascular events, and decreased mobility [43, 48, 49]. Mortality rates are also notable, with 30-day mortality ranging from 2.8 to 12.1% and one-year mortality between 14% and 36% [43, 48, 49]. In Taiwan, postoperative pain management follows standardized protocols, including multimodal analgesia with opioids, NSAIDs, and regional anesthesia when applicable. These factors highlight the severity of this surgery and its substantial impact on older patients. To reduce potential bias, we excluded patients who underwent other surgeries, multiple hip fracture surgeries, or had missing baseline information, as outlined in Table 1. These exclusions were necessary to ensure consistency in surgical procedures and to minimize potential biases that may arise from varying risks of postoperative hyperactive delirium and death during the follow-up period. No patients with preoperative delirium were included in the postoperative hyperactive delirium group, as our exclusion criteria explicitly omitted patients with delirium before the index surgery date.

We classified the enrolled patients into two groups according to their postoperative hyperactive delirium status following hip fracture surgery: Group 1 comprised 263,642 older patients without postoperative hyperactive delirium, and Group 2 included 6,795 patients who received a postoperative hyperactive delirium diagnosis (see Table 1). Patients in the hyperactive delirium group were exclusively those diagnosed with hyperactive delirium by ICU intensivists or anesthesiologists specializing in critical care. For the control group, patients with hypoactive or mixed delirium were excluded to maintain the integrity of the comparison. Therefore, the control group included only patients without any delirium diagnosis. This rigorous classification ensured the elimination of heterogeneity in the control group, addressing potential biases.

Postoperative hyperactive delirium

In our study conducted in Taiwan, the diagnosis of postoperative hyperactive delirium was based on the 3-Minute Diagnostic Confusion Assessment Method (3D-CAM) scale, performed by psychiatric, anesthesia, or surgical physicians. The assessments were conducted daily during ICU rounds or whenever clinically indicated, ensuring consistency throughout the ICU stay. The timing and frequency of these evaluations were standardized across all participating institutions. Our study focused specifically on the hyperactive subtype of delirium that required pharmacological treatment. Diagnosis involved identifying significant changes in mental status, such as agitation or incoherent speech, with a primary emphasis on the hyperactive subtype warranting medication. Our main objective was to investigate the relationship between hyperactive delirium and mortality. We defined postoperative hyperactive delirium as delirium occurring after surgery and requiring the administration of specific medications, such as antipsychotics, benzodiazepines, and sedative-hypnotics. The medications used to manage

Table 1 Comparison of characteristics between postoperative hyperactive delirium and non-delirium groups in older patients receiving hip fracture surgery

	Before propensity scores patching					After propensity scores patching				
	Non-delirium		Delirium		ASMD	Non-delirium		Delirium		ASMD
	N = 24,786		*N* = 6,795			*N* = 6,795		*N* = 6,795		
	N	%	N	%		N	%	N	%	
Age (mean ± SD), years-old	75.11 ± 12.54		78.07 ± 11.44			78.01 ± 10.22		78.07 ± 11.44		
Age group, years-old					0.3490					0.0270
Group 1: 65–70	7,361	29.7%	2,054	30.2%		2,110	31.1%	2,054	30.2%	
Group 2: 71–75	6,915	27.9%	1,114	16.4%		1,068	15.7%	1,114	16.4%	
Group 3: 76–80	5,701	23.1%	1,482	21.8%		1,514	22.3%	1,482	21.8%	
Group 4: >80	4,809	19.4%	2,145	31.6%		2,103	31.0%	2,145	31.6%	
Sex					0.3132					0.0111
Female	13,533	54.6%	2,660	39.2%		2,697	39.7%	2,660	39.2%	
Male	11,253	45.4%	4,135	60.9%		4,098	60.3%	4,135	60.9%	
Income levels (NTD)					0.3430					0.0440
Unemployment	198	0.8%	159	2.3%		136	2.0%	159	2.3%	
Financial dependent	7,014	28.3%	2,667	39.3%		2,782	40.9%	2,667	39.3%	
≦20,000	7,932	32.0%	2,177	32.0%		2,159	31.8%	2,177	32.0%	
2000–30,000	4,932	19.9%	1,119	16.5%		1,094	16.1%	1,119	16.5%	
30,000–45,000	2,999	12.1%	456	6.7%		425	6.3%	456	6.7%	
>45,000	1,711	6.9%	217	3.2%		199	2.9%	217	3.2%	
Urbanization					0.1038					0.0314
Rural	6,519	26.3%	2,108	31.0%		2,207	32.5%	2,108	31.0%	
Urban	18,267	73.7%	4,687	69.0%		4,588	67.5%	4,687	69.0%	
ASA physical status					0.5530					0.0280
1	15,913	64.2%	2,960	43.6%		3,000	44.2%	2,960	43.6%	
2	3,445	13.9%	986	14.5%		1,028	15.1%	986	14.5%	
3	4,387	17.7%	1,532	22.6%		1,508	22.2%	1,532	22.6%	
4	1,041	4.2%	1,317	19.4%		1,259	18.5%	1,317	19.4%	
Types of anesthesia					0.6349					0.0180
General anesthesia	15,615	63.0%	6,039	88.9%		6,077	89.4%	6,039	88.9%	
Regional anesthesia	9,171	37.00%	756	11.1%		718	10.6%	756	11.1%	
Duration of anesthesia					0.2922					0.0011
≤ 2 h	22,530	90.9%	5,830	85.8%		5,833	85.8%	5,830	85.8%	
> 2 h	2,256	9.1%	965	14.2%		962	14.2%	965	14.2%	
Pre-existing comorbidity										
Diabetes	2,305	9.3%	1,034	15.2%	0.1829	974	14.3%	1,034	15.2%	0.0251
Hypertension	4,610	18.6%	2,115	31.1%	0.2938	2,008	29.6%	2,115	31.1%	0.0344
Hyperlipidemia	2,652	10.7%	986	14.5%	0.1153	927	13.6%	986	14.5%	0.0250
Coronary artery disease	2,032	8.2%	971	14.3%	0.1922	914	13.5%	971	14.3%	0.0243
Stroke	1,363	5.5%	1,355	19.9%	0.4431	1,262	18.6%	1,355	19.9%	0.0348
Depression	967	3.9%	589	8.7%	0.1985	563	8.3%	589	8.7%	0.0136
Anxiety	1,909	7.7%	792	11.7%	0.1357	728	10.7%	792	11.7%	0.0301
Heart failure	471	1.9%	343	5.1%	0.1753	328	4.8%	343	5.1%	0.0102
Peripheral vascular disease	570	2.3%	401	5.9%	0.1854	399	5.9%	401	5.9%	0.0013
COPD	2,503	10.1%	1,081	15.9%	0.1750	1,065	15.7%	1,081	15.9%	0.0066
Atrial fibrillation	174	0.7%	148	2.2%	0.1266	116	1.7%	148	2.2%	0.0340
Traumatic head injury	1,685	6.8%	775	11.4%	0.2652	773	11.4%	775	11.4%	0.0009
Alcohol liver diseases	521	2.1%	421	6.2%	0.1981	418	6.2%	421	6.2%	0.0008
Cognitive function decline	446	1.8%	428	6.3%	0.3391	429	6.3%	428	6.3%	0.0002
Sleep Disorder	3,495	14.1%	1,393	20.5%	0.4091	1,390	20.5%	1,393	20.5%	0.0011
Malnutrition	1,760	7.1%	836	12.3%	0.2094	833	12.3%	836	12.3%	0.0010
CCI Scores										
Median (IQR, Q1-Q3)	0.00 (0.00,0.00)		0.00 (0.00,1.00)			0.00 (0.00,1.00)		0.00 (0.00,1.00)		

Table 1 (continued)

	Before propensity scores patching					After propensity scores patching				
	Non-delirium		Delirium		ASMD	Non-delirium		Delirium		ASMD
	N = 24,786		*N* = 6,795			*N* = 6,795		*N* = 6,795		
	N	%	N	%		N	%	N	%	
CCI Scores					0.3290					0.0025
0	19,730	79.6%	4,419	65.0%		4,427	65.2%	4,419	65.0%	
≥ 1	5,056	20.4%	2,376	35.0%		2,368	34.9%	2,376	35.0%	
CCI										
Congestive Heart Failure	397	1.6%	324	4.8%	0.1784	286	4.2%	324	4.8%	0.0270
Dementia	324	1.3%	256	3.8%	0.2296	250	3.7%	256	3.8%	0.0008
Chronic Pulmonary Disease	2,008	8.1%	890	13.1%	0.1640	980	14.4%	890	13.1%	0.0383
Rheumatic Disease	149	0.6%	47	0.7%	0.0087	61	0.9%	47	0.7%	0.0236
Liver Disease	2,132	8.6%	771	11.4%	0.0926	854	12.6%	771	11.4%	0.0376
Diabetes with complications	471	1.9%	230	3.4%	0.0960	231	3.4%	230	3.4%	0.0011
Hemiplegia and Paraplegia	3	0.0%	1	0.0%	0.0141	1	0.0%	1	0.0%	0.0000
Renal Disease	421	1.7%	254	3.7%	0.1293	258	3.8%	254	3.7%	0.0032
AIDS	8	0.0%	6	0.1%	0.0196	5	0.1%	6	0.1%	0.0071
Cancer	545	2.2%	486	7.2%	0.2349	479	7.0%	486	7.2%	0.0004
Outcomes					***P*Value**					***P*Value**
All-Cause Death	2,726	11.0%	1,815	26.7%	< 0.0001	1,360	20.0%	1,815	26.7%	< 0.0001
Mean (SD) follow-up year	8.45 ± 4.94		7.04 ± 5.09		< 0.0001	7.59 ± 4.95		7.04 ± 5.09		< 0.0001

Abbreviations: ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; ASMD, absolute standardized mean difference; IQD, interquartile range; SD, standard deviation; COPD, Chronic Obstructive Pulmonary Disease; N, Number; NTD, New Taiwan Dollars

Statistical test: Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate

Continuous variables were analyzed using independent t-tests for normally distributed data and the Wilcoxon rank-sum test for non-normally distributed data

postoperative hyperactive delirium, including antipsychotics, benzodiazepines, and sedative-hypnotics, were recorded in the NHIRD. These pharmacological interventions, when combined with ICD codes, improved diagnostic accuracy and ensured robust case identification. Of note, we acknowledge that hypoactive delirium is inherently more challenging to diagnose, even for experienced ICU specialists. Despite this limitation, we took every possible step to exclude hypoactive delirium cases during the analysis to enhance the reliability of our findings. Our analysis excluded delirium types such as hypoactive or mixed, with pharmacological interventions primarily targeting the hyperactive or agitated subtype.

Rationale for five-year follow-up

The decision to focus on five-year outcomes reflects our aim to assess the extended impact of postoperative hyperactive delirium on patient survival in this vulnerable population. Short-term outcomes, such as 30-day or 90-day mortality, often capture immediate complications but may not account for the prolonged effects of delirium, such as functional decline, cognitive deterioration, and chronic health issues. By selecting a five-year follow-up, we aimed to evaluate these lasting implications, providing a robust understanding of the long-term risks associated with postoperative hyperactive delirium. The five-year timeframe was also chosen due to the availability and completeness of data in the NHIRD, enabling detailed and clinically relevant analyses.

Propensity score matching and covariates

To ensure the validity and reliability of our study's findings, we employed a comprehensive range of statistical methods designed to minimize the impact of potential confounders. To begin with, we performed 1:1 PSM with a caliper of 0.1 for a variety of variables that are known to influence mortality in patients receiving hip fracture surgery, as outlined in Table 1 [50, 51]. These variables included age, sex, income levels, urbanization, American Society of Anesthesiologists (ASA) physical status, types and duration of anesthesia, pre-existing comorbidity, and Charlson Comorbidity Index (CCI) scores (shown in Table 1). We then used Cox proportional hazards models to evaluate the impact of postoperative hyperactive delirium on all-cause mortality in older patients receiving hip fracture surgery. To account for clustering within matched sets, we utilized robust sandwich estimators. We conducted multivariate Cox regression analyses to calculate hazard ratios (HRs) for the mortality associated with postoperative hyperactive delirium in patients undergoing hip fracture surgery. Comorbidities were identified using ICD-9-CM or ICD-10-CM codes for main diagnoses in inpatient records or outpatient visits occurring at least twice within one year. Continuous variables were presented as means ± standard deviations,

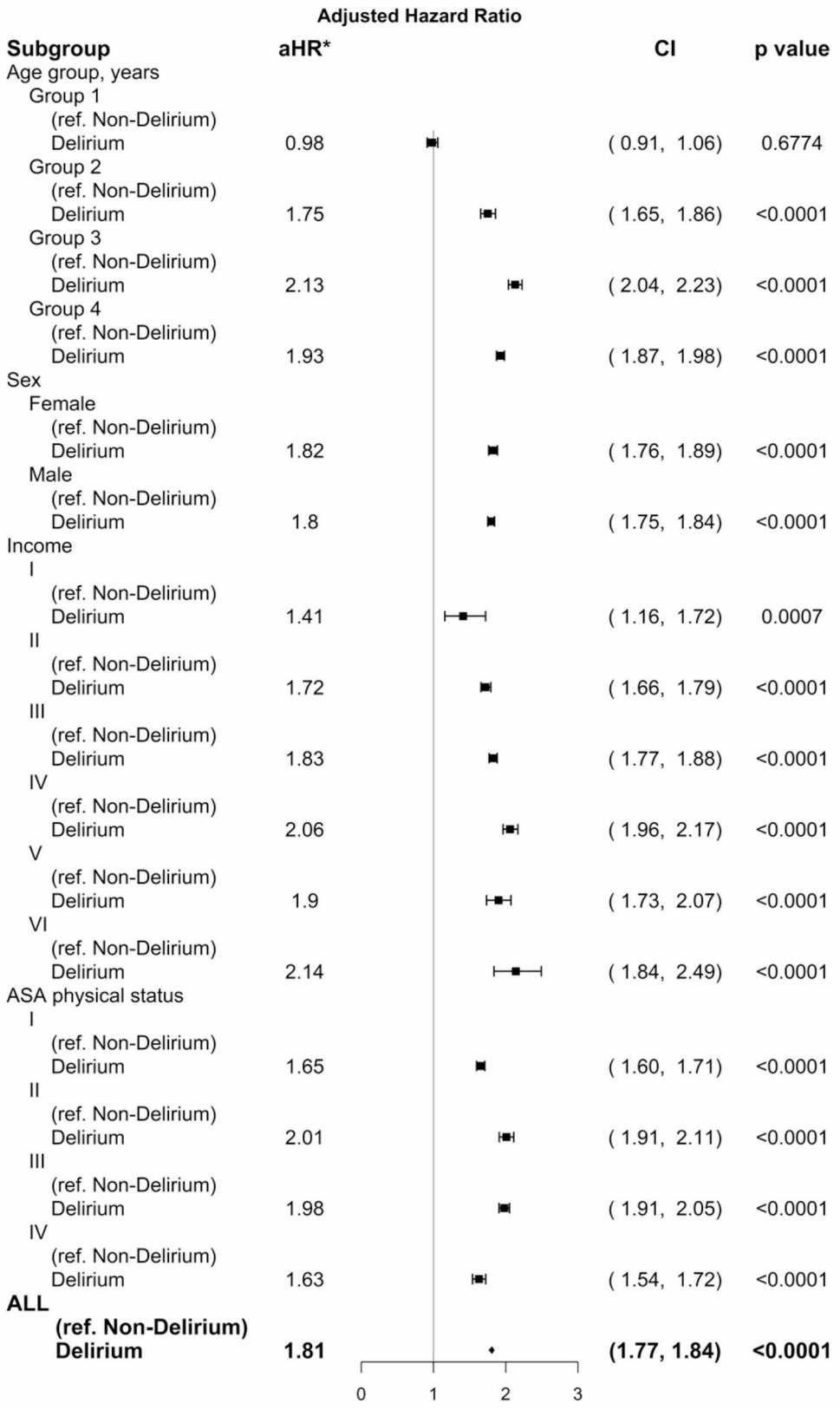

Fig. 1 (See legend on next page.)

(See figure on previous page.)

Fig. 1 Subgroup analysis of all-cause mortality in older patients undergoing hip fracture surgery with and without postoperative hyperactive delirium using inverse probability of treatment weighting. Footnote: Adjustment of age, sex, income levels, urbanization, elective status, ASA physical status, types of anesthesia, duration of anesthesia, coexisting comorbidity, and CCI scores. Abbreviations: aHR = adjusted hazard ratio; CI = confidence interval; ASA = American Society of Anesthesiologists. Statistical method: Subgroup analysis was conducted using inverse probability of treatment weighting (IPTW) to adjust for confounding variables and ensure balance between comparison groups

where appropriate. Our study's implementation of these rigorous statistical approaches provides a reliable assessment of the mortality risk associated with postoperative hyperactive delirium in patients undergoing hip fracture surgery in real-world settings.

Subgroup analysis

Subgroup analysis can provide valuable insights into how specific patient characteristics influence outcomes in different populations. In our study, we conducted a subgroup analysis to investigate the impact of postoperative hyperactive delirium on all-cause mortality rates in older patients undergoing hip fracture surgery. Subgroup analyses were conducted to explore whether the relationship between postoperative hyperactive delirium and all-cause mortality varied across patient characteristics, including age, sex, income levels, and ASA physical status. These characteristics were selected based on their known associations with delirium and mortality risk. The analyses used inverse probability of treatment weighting (IPTW) with adjustments for all covariates to ensure robust estimates of the mortality risk attributable to postoperative hyperactive delirium within each subgroup. This approach minimized the impact of potential confounding factors and provided a comprehensive understanding of how different patient characteristics influence outcomes, as detailed in Table 1 [51, 52].

Statistical analysis

To ensure the robustness and credibility of our findings, we employed SAS version 9.4 (SAS Institute, Cary, NC, USA) for all statistical analyses, including comprehensive adjustments for potential confounding factors. Statistical significance was defined as $P < 0.05$ using a two-tailed Wald test. In Table 1, categorical variables were compared using the Chi-square test or Fisher's exact test, while continuous variables were analyzed using independent t-tests for normally distributed data and the Wilcoxon rank-sum test for non-normally distributed data.

To further validate our findings, subgroup analyses were conducted using inverse probability of treatment weighting (IPTW) in Fig. 1, ensuring balance between comparison groups. We conducted a power analysis to confirm that our study was adequately powered to detect meaningful differences in mortality. The required sample size was estimated based on a hazard ratio of 1.6, with 80% power and a significance level of 0.05. Our final sample size exceeded this threshold, supporting the robustness and reliability of our findings.

To evaluate overall survival in Fig. 2, we utilized the Kaplan-Meier method, and differences between groups were assessed using the stratified log-rank test, accounting for matched sets within the PSM cohort. Additionally, Cox proportional hazards models with robust sandwich estimators, as presented in Table 2, were used to estimate HRs and 95% confidence intervals (CIs) while accounting for clustering within matched sets [53].

Results

Study cohorts before and after PSM

During the period from 2008 to 2018, we identified 31,581 older patients who underwent emergency hip fracture surgery. Among these patients, 97.5% ($n = 24{,}786$) did not develop postoperative hyperactive delirium, whereas 21.5% ($n = 6{,}795$) did develop the condition (Table 1). The postoperative hyperactive delirium group was characterized by a higher proportion of older adults, males, individuals with lower income levels, and more rural residents. Additionally, this group was more likely to have undergone emergency surgery, have higher ASA scores, longer duration of anesthesia, more pre-existing comorbidities, and higher CCI scores than the group without postoperative hyperactive delirium. Prior to PSM, the all-cause mortality rate was 26.75% and 11.0% ($P < 0.0001$) for the postoperative hyperactive delirium and no postoperative hyperactive delirium groups, respectively (Table 1).

After implementing PSM, we included 13,590 patients (6,795 in each group) for further analysis, achieving balance between groups in age, sex, income levels, urbanization, ASA physical status, types and duration of anesthesia, pre-existing comorbidity, and CCI scores with absolute standardized mean differences of less than 0.1. Following PSM, we observed a higher crude rate of all-cause death in the postoperative hyperactive delirium group (26.7%) compared to the no postoperative hyperactive delirium group (20.0%), which was statistically significant ($P < 0.0001$) (Table 1).

Cox proportional hazard models of all-cause death

Before PSM, we adjusted for potential confounding factors, such as age, sex, income levels, urbanization, ASA physical status, types of anesthesia, duration of anesthesia, pre-existing comorbidity, and CCI scores, using Cox proportional hazards models to estimate the aHRs for

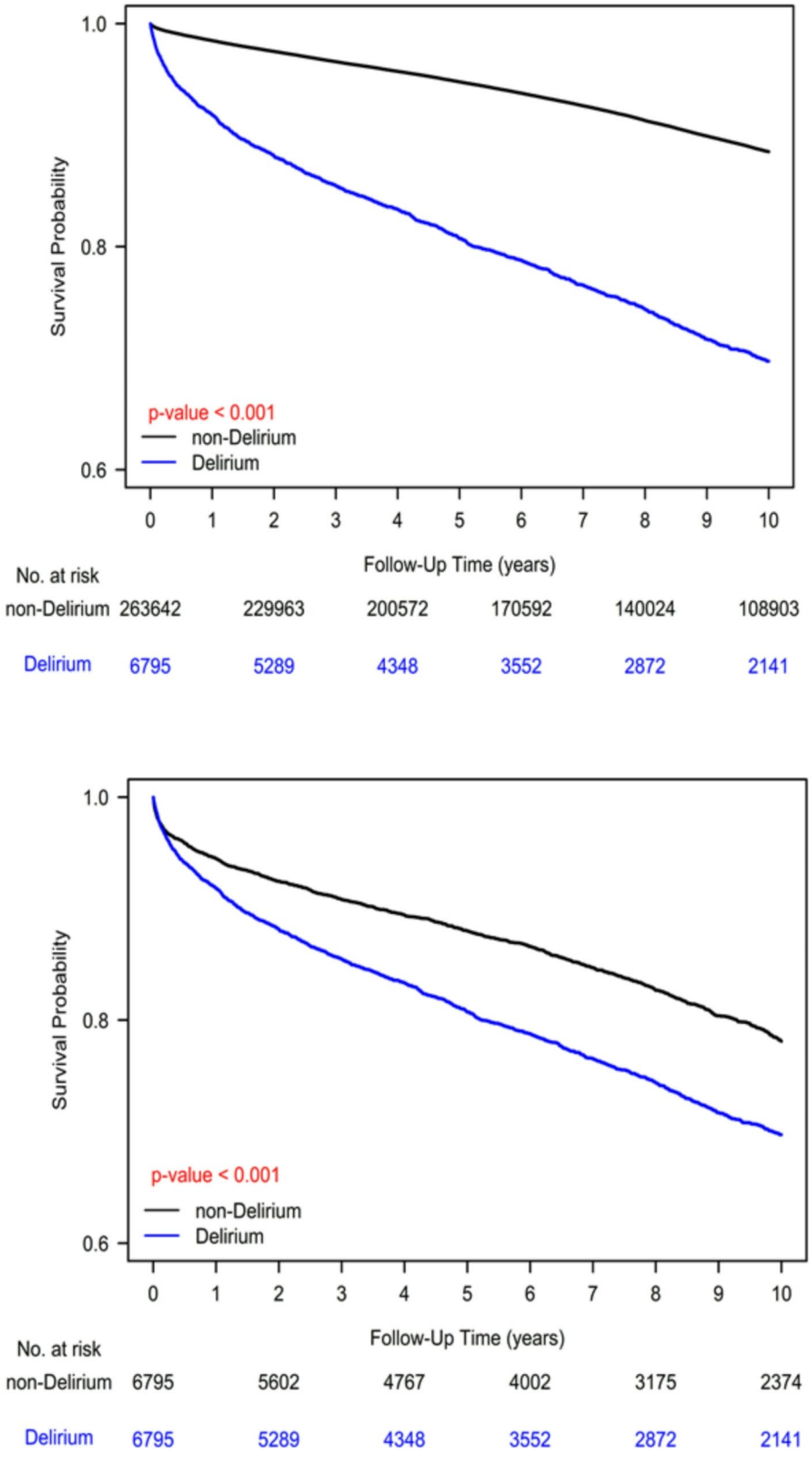

Fig. 2 Kaplan-meier analysis of overall survival in hip fracture surgery older patients with and without postoperative hyperactive delirium. (2**A**) Before propensity scores patching (2**B**) After propensity scores patching. Statistical test: Kaplan-Meier analysis was used to estimate overall survival, and the stratified log-rank test was applied to compare survival distributions while accounting for matched sets

Table 2 A cox proportional regression model of mortality risk in older patients receiving hip fracture surgery with and without postoperative hyperactive delirium

	Crude HR(95% CI)		*P*-value	Adjusted HR* (95% CI)		*P*-value
	Model 1: Before propensity scores patching					
No Postoperative hyperactive delirium (ref.)	1.00			1.00		
Postoperative hyperactive delirium	2.93	(2.80, 3.08)	< 0.0001	1.72	(1.64, 1.81)	< 0.0001
	Model 2: After propensity scores patching					
No Postoperative hyperactive delirium (ref.)	1.00					
Postoperative hyperactive delirium	1.42	(1.32, 1.52)	< 0.0001	1.62	(1.51, 1.74)	< 0.0001

Abbreviations: HR, hazard ratios; CI, confidence interval

Adjustment of age, sex, income levels, urbanization, elective status, ASA physical status, types of anesthesia, duration of anesthesia, coexisting comorbidity, and CCI scores

Statistical test: The Cox proportional hazards model with robust sandwich estimators was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) while accounting for clustering within matched sets

all-cause death. The results revealed that patients who developed postoperative hyperactive delirium following hip fracture surgery had a significantly higher risk of mortality compared to those who did not (adjusted HR, 1.72; 95% confidence interval [CI], 1.64–1.81; $P < 0.0001$) (Table 2).

After conducting PSM, we further investigated the relationship between postoperative hyperactive delirium and mortality risk using multivariate Cox regression analysis, as detailed in Table 2. Univariate and multivariate analyses consistently demonstrated that postoperative hyperactive delirium was a significant risk factor for all-cause mortality in older patients who underwent emergency hip fracture surgery. Specifically, the aHR (95% CIs) for all-cause mortality was 1.62 (95% CI, 1.51–1.74; $P < 0.0001$) in the postoperative hyperactive delirium group compared to the no postoperative hyperactive delirium group. These results indicate that postoperative hyperactive delirium is an independent risk factor for all-cause death in older patients after hip fracture surgery, even after adjusting for potential confounding variables.

Subgroup analysis

The results of the subgroup analysis of all-cause mortality in patients undergoing hip fracture surgery with and without postoperative hyperactive delirium are shown in Fig. 1. Using IPTW with adjustment for all covariates shown in Table 1, the adjusted hazard ratios (aHRs) of all-cause death for older patients with postoperative hyperactive delirium were significantly higher than those without postoperative hyperactive delirium, regardless of age, sex, income levels, or ASA scores. Subgroup analysis revealed that postoperative hyperactive delirium was associated with significantly higher adjusted hazard ratios for all-cause death across most subgroups, demonstrating that this condition independently increases mortality risk regardless of baseline characteristics, such as age, sex, ASA physical status, and income level. The overall aHR (95% CI) of all-cause death for the postoperative hyperactive delirium group by IPTW was 1.81 (95% CI, 1.77–1.84; $P < 0.0001$).

Kaplan–Meier curves of overall survival

The overall survival rate was significantly higher in patients without postoperative hyperactive delirium compared to those with delirium before PSM, as evidenced by the Kaplan-Meier curve (Fig. 2A, $P < 0.001$). Specifically, the 5-year overall survival rates were 94.9% and 81.7% for the no postoperative hyperactive delirium and postoperative hyperactive delirium groups, respectively, in patients who underwent hip fracture surgery. After PSM, the matched groups were further analyzed using Kaplan-Meier curves to evaluate overall survival (Fig. 2B). The results also demonstrated a significant difference in overall survival between the postoperative hyperactive delirium and no postoperative hyperactive delirium groups (Fig. 2B, $P < 0.001$), with 5-year overall survival rates of 89.8% and 81.7%, respectively. These findings suggest that postoperative hyperactive delirium is associated with a lower overall survival rate, even after PSM.

Discussion

The association between postoperative hyperactive delirium and mortality is an area of increasing research interest, but the presence of confounding bias makes causal inference challenging [9, 35–40]. Many factors that are strongly associated with postoperative hyperactive delirium, such as advanced age, comorbidity, and high-risk surgery, are also independent risk factors for mortality [7, 23, 24]. Therefore, the quality of observational studies is critical for accurate estimation of the impact of postoperative hyperactive delirium on mortality. Additionally, we recognize the importance of distinguishing between hyperactive and hypoactive delirium in understanding mortality-related outcomes. While both subtypes share common risk factors such as advanced age, comorbidities, and preexisting cognitive impairment, each presents unique clinical challenges and subtype-specific

precipitating factors [7, 23, 24]. Hyperactive delirium, characterized by overt symptoms like agitation and restlessness, is often linked to withdrawal syndromes, acute neurologic events, or medication-related triggers [54–56]. Conversely, hypoactive delirium, marked by subtle presentations such as lethargy and reduced responsiveness, is more frequently associated with metabolic disturbances, hypoactive infections, or undetected organ failure [57, 58]. These differences not only influence diagnostic accuracy but also likely contribute to variations in long-term mortality outcomes. While our study focuses on hyperactive delirium due to its higher diagnostic reliability in large datasets [20–22], future research should explore the differential impacts of delirium subtypes on long-term survival to better inform tailored clinical strategies. Previous studies have had limitations, including small sample sizes, inhomogeneous surgical types, and focus on short-term mortality [9, 35–40]. To address these limitations, we conducted the first and largest PSM cohort study to evaluate the association between postoperative hyperactive delirium and long-term survival in older patients receiving emergency hip fracture surgery with the same surgical procedure and anesthesia type. Our results showed that postoperative hyperactive delirium was an independent risk factor for all-cause death, with an adjusted hazard ratio of 1.62 (95% CI, 1.51–1.74; $P<0.0001$) after PSM. Subgroup analysis revealed that older patients receiving hip fracture surgery with postoperative hyperactive delirium in all subgroups had significantly higher adjusted hazard ratios of all-cause death compared with those without postoperative hyperactive delirium, regardless of age, sex, income levels, or ASA scores. The overall adjusted hazard ratio of all-cause death for the postoperative hyperactive delirium group by IPTW was 1.81 (95% CI, 1.77–1.84; $P<0.0001$). Additionally, the 5-year overall survival rate was lower in the postoperative hyperactive delirium group than in the no postoperative hyperactive delirium group, at 81.7% and 89.8%, respectively, in patients who underwent hip fracture surgery after PSM. Our subgroup analysis highlights patient groups, such as those with advanced age or higher ASA physical status, that are at greater risk of mortality associated with postoperative hyperactive delirium. While our study did not evaluate interventions, these findings could guide future research to develop targeted prevention and management strategies.

The previous studies that examined the relationship between postoperative hyperactive delirium and mortality have been of varying quality, leading to conflicting conclusions. For example, a small study conducted by Gottschalk et al. that included 459 patients aged 65 years or older with hip fractures did not find a significant independent association between incident postoperative hyperactive delirium and mortality [37]. However, the small sample size and lack of consideration for major comorbidities associated with all-cause death in the study might have led to poor quality of evidence [37]. In contrast, Dubljanin-Raspopović et al. found that in a population of 384 older patients with hip fractures, postoperative hyperactive delirium was an independent predictor of 30-day mortality. [38, 39] The divergent findings may be partly explained by differences in confounding variables considered in the studies [37–39]. Although both studies adjusted for age, sex, and ASA score, Gottschalk et al. additionally controlled for preexisting cognitive function decline [37], while Dubljanin-Raspopović et al. [38, 39] did not account for baseline cognitive function, which is the strongest known predictor of delirium and an independent predictor of postoperative mortality [2–5]. This comparison highlights the potential fragility of the delirium-mortality association depending on the choice of confounders included in adjusted models [37–39]. Furthermore, some meta-analysis of low-quality studies including those on surgeries other than hip fractures suggested that postoperative hyperactive delirium is a risk factor for short-term mortality (6–12 months) [36, 40]. However, the quality of evidence from the studies included in the meta-analysis is uncertain, as the "garbage in, garbage out" theory applies [36, 40]. Therefore, the impact of postoperative hyperactive delirium on long-term mortality in older patients who receive the same surgical type and emergency anesthesia remains unclear.

PSM can be particularly useful in situations where a randomized controlled trial (RCT) is not feasible [59, 60], such as in the case of postoperative hyperactive delirium in our study, which is a disease state and not an intervention. PSM offers several advantages, including reducing bias, creating a better balance between groups, improving precision, and being considered a more ethical approach [60]. Matching cases and controls based on their propensity scores creates more comparable groups, reducing the potential for bias and allowing for more accurate comparisons (Table 1) [60, 61]. Additionally, PSM can improve the precision of estimates by reducing the variability of estimates in the sample [61]. However, it is important to know that PSM has limitations, including potential loss of information due to the exclusion of unmatched cases, sensitivity to the choice of covariates and matching algorithm, and the possibility of residual confounding [62]. These limitations can lead to biased estimates and reduced generalizability of results [62]. To overcome the limitations of PSM, we also employed Cox regression modeling for the cohort before PSM (Table 2), and IPTW for subgroup analysis (Fig. 1) [63, 64]. In this large older cohort study, we found that postoperative hyperactive delirium in older patients receiving hip fracture surgery was associated with an increased risk of

long-term mortality (Table 2; Fig. 1, and Fig. 2), regardless of the analytical method used, including PSM, Cox regression, or IPTW analysis in the subgroup analysis.

Postoperative hyperactive delirium is a common complication in older patients undergoing surgery, particularly those with preexisting cognitive impairment or dementia [2–5]. The mechanisms of the association between postoperative hyperactive delirium in the older patients receiving hip fracture surgery and increased mortality risk might be the following reasons. Postoperative hyperactive delirium can lead to a prolonged hospital stay [9], which in turn can increase the risk of complications such as infection and thrombosis [10, 11]. This can have a negative impact on the patient's overall health status and increase the risk of mortality. Additionally, postoperative hyperactive delirium is associated with a decline in functional status and cognitive function, which can lead to long-term disability and a reduced quality of life [12]. This can contribute to the development of other chronic conditions, such as depression, and ultimately increase the risk of mortality [13]. Moreover, postoperative hyperactive delirium can lead to an increased risk of falls and injuries, which can further contribute to disability and mortality risk [14]. Finally, postoperative hyperactive delirium is often associated with other medical complications, such as electrolyte imbalances and respiratory failure, which can also increase the risk of mortality [6–8]. Overall, the mechanisms by which postoperative hyperactive delirium increases mortality risk are complex and multifactorial, but likely involve a combination of physiological, psychological, and social factors.

Our study use the largest cohort study to show postoperative hyperactive delirium in older patients undergoing emergency hip fracture surgery has been shown to be associated with increased risk of long-term mortality (Table 2; Fig. 1, and Fig. 2). To prevent the risk of mortality and improve related health policies, several strategies can be employed. First, preoperative risk assessment and optimization of comorbidities can reduce the risk of postoperative hyperactive delirium [1]. Second, measures can be taken to prevent delirium in the postoperative period, including early mobilization, adequate pain management, and avoidance of sedatives and other medications that can contribute to delirium [14]. Third, timely diagnosis and treatment of delirium can improve outcomes and reduce mortality [15]. In terms of health policy, efforts can be made to improve the quality of care for older patients undergoing hip fracture surgery, including the implementation of best practices for delirium prevention and management, as well as improving access to rehabilitation and postoperative care [16]. Additionally, there may be a role for healthcare systems to incentivize hospitals and providers to deliver high-quality care for this vulnerable population [17]. Based on our study, we suggest preventing postoperative hyperactive delirium and improving its management in older patients undergoing emergency hip fracture surgery may lead to improved outcomes and reduced mortality, as well as improved health policies and care delivery [1, 14–17].

There were some strength in our study. Firstly, our study has a largest sample size of older patients receiving emergency hip fracture surgery with long-term follow up, which enhances the statistical power of our analysis. Secondly, we used multiple methods including PSM, Cox regression model before and after PSM, and IPTW analysis to control for confounding variables and obtain more accurate estimates of the effect of postoperative hyperactive delirium on mortality (Table 2; Fig. 2). Thirdly, our study was conducted in a real-world clinical setting, which increases the generalizability of our findings to other similar settings. Fourthly, we used a long-term follow-up period of up to 7–8 years, which enabled us to examine the long-term impact of postoperative hyperactive delirium on mortality in this patient population. Finally, our study provides important insights into the mechanisms underlying the association between postoperative hyperactive delirium and mortality in older patients receiving emergency hip fracture surgery, which may inform the development of targeted interventions to prevent postoperative hyperactive delirium and improve patient outcomes [1, 14–17].

There are several limitations to our study that warrant consideration. First, our study was conducted using data from a single healthcare system in Taiwan, which may limit the generalizability of our findings to other regions or countries. Second, as with all retrospective studies, our study is susceptible to selection bias and other potential limitations inherent in the study design. Despite this, given the difficulty in conducting randomized controlled trials on this issue, we believe that our study provides valuable insights into the relationship between postoperative hyperactive delirium and long-term mortality. Third, while we made efforts to adjust for potential confounding factors using PSM, it is possible that there were other unmeasured confounding variables that could have affected our results. Fourth, our study only focused on older patients undergoing emergency hip fracture surgery, and the findings may not be generalizable to other populations or surgical procedures. Fifth, the NHIRD does not provide detailed information on the duration or severity of postoperative hyperactive delirium. As a result, our study could not evaluate whether the severity or duration of postoperative hyperactive delirium impacts mortality outcomes. This lack of granular data limits our ability to fully understand the relationship between delirium characteristics and long-term mortality. Sixth, our study faced the difficulty in diagnosing

hypoactive delirium, which is often underdiagnosed due to its subtle presentation [20–22], whereas hyperactive delirium's overt symptoms allow for more precise diagnoses [18, 19, 49, 65]. While the association between hyperactive delirium and mortality is statistically significant, its clinical relevance is less clear given the high overall mortality in both groups. Ethical and practical challenges of conducting RCTs highlight the value of our database-driven analysis in understanding long-term implications of delirium subtypes [18, 19, 49, 65]. Despite these limitations, we believe that our study is of high quality due to the well-matched large cohort established by PSM and the inclusion of important confounding variables such as delirium, cognitive function, dementia, and other potential preexisting comorbidities.

There are several limitations to our study that warrant consideration. First, our study was conducted using data from a single healthcare system in Taiwan, which may limit the generalizability of our findings to other regions or countries. Second, as with all retrospective studies, our study is susceptible to selection bias and other potential limitations inherent in the study design. Despite this, given the difficulty in conducting randomized controlled trials on this issue, we believe that our study provides valuable insights into the relationship between postoperative hyperactive delirium and long-term mortality. Third, while we made efforts to adjust for potential confounding factors using PSM, it is possible that there were other unmeasured confounding variables that could have affected our results. Fourth, our study only focused on older patients undergoing emergency hip fracture surgery, and the findings may not be generalizable to other populations or surgical procedures. Fifth, our study is the difficulty in diagnosing hypoactive delirium, often underdiagnosed due to its subtle presentation [20–22], whereas hyperactive delirium's overt symptoms allow for more precise diagnoses [18, 19, 49, 65]. While the association between hyperactive delirium and mortality is statistically significant, its clinical relevance is less clear given the high overall mortality in both groups. Ethical and practical challenges of conducting RCTs highlight the value of our database-driven analysis in understanding long-term implications of delirium subtypes [49, 65]. Despite these limitations, we believe that our study is of high quality due to the well-matched large cohort established by PSM and the inclusion of important confounding variables such as delirium, cognitive function, dementia, and other potential preexisting comorbidities.

Conclusion

Postoperative hyperactive delirium is independently associated with an increased risk of long-term mortality in older patients undergoing emergency hip fracture surgery, underscoring its clinical significance. These findings highlight the need for increased attention to the prevention, early diagnosis, and tailored management of delirium in this vulnerable population to mitigate adverse outcomes and reduce mortality risk. Furthermore, future studies should explore the impact of other delirium subtypes, such as hypoactive and mixed delirium, to provide a more comprehensive understanding of their roles in patient outcomes.

Abbreviations

PSM	Propensity score matching
NHI	National Health Insurance
NHIRD	National health insurance research database
ICD-9-CM	International classification of diseases, ninth revision, clinical modification
ICD-10-CM	International classification of diseases, tenth revision, clinical modification
ASA	American society of anesthesiologists
CCI	Charlson comorbidity index
HR	Hazard ratios
IPTW	Inverse probability of treatment weighting
n	Number
CI	Confidence interval
RCT	Randomized controlled trial

Acknowledgements

Not applicable.

Author contributions

Conception and Design: MS, WMC, SYW, JZ. Collection and Assembly of Data: SYW, JZ. Data Analysis and Interpretation: JZ, SYW. Administrative Support: SYW. Manuscript Writing: MS, WMC, SYW, JZ. Final Approval of Manuscript: All authors.

Funding

This work was supported by the Lo-Hsu Medical Foundation, Lotung Poh-Ai Hospital (Funding Numbers: 11403, 11404) for SYW's contribution. Additionally, JZ received support from the Henan Young and Middle-Aged Health Academic Leader Project (Nos. CYQ20210026), and MS received support from the same project (Nos. CYQ20220019). The sponsors had no role in the design, execution, interpretation, or publication of this study.

Data availability

The data sets supporting the study conclusions are included in the manuscript. We used data from the National Health Insurance Research Database and Taiwan Cancer Registry database. The authors confirm that, for approved reasons, some access restrictions apply to the data underlying the findings. The data used in this study cannot be made available in the manuscript, the supplemental files, or in a public repository due to the Personal Information Protection Act executed by Taiwan's government, starting in 2012. Requests for data can be sent as a formal proposal to obtain approval from the ethics review committee of the appropriate governmental department in Taiwan. Specifically, links regarding contact info for which data requests may be sent to are as follows: http://nhird.nhri.org.tw/en/Data_Subsets.html#S3 and http://nhis.nhri.org.tw/point.html.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) of Tzu-Chi Medical Foundation (Approval Number: IRB109-015-B). As this study was conducted using fully de-identified, real-world big data from the National Health Insurance Research Database (NHIRD) and the Taiwan Cancer Registry Database, individual informed consent was not required. The datasets were de-identified in strict compliance with Taiwan's Personal Information Protection Act, and no direct patient interactions or interventions were involved. Therefore, the IRB granted a waiver for informed consent. Furthermore, this study adhered to the ethical principles outlined in the

Declaration of Helsinki, ensuring the protection, confidentiality, and ethical use of patient data throughout the research process. Access to the NHIRD dataset was granted through formal application and approval from the relevant regulatory authorities.

Consent for publication
Not applicable.

Informed consent
Informed consent was waived because the data sets are covered under the Personal Information Protection Act. Szu-Yuan Wu, MD, PhD had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The data has not been previously presented orally or by poster at scientific meetings.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Anesthesiology and Perioperative Medicine, Henan Provincial People's Hospital, People's Hospital of Zhengzhou University, No.7. Weiwu Road, Zhengzhou, Henan, China
[2]Graduate Institute of Business Administration, College of Management, Fu Jen Catholic University, Taipei, Taiwan
[3]Artificial Intelligence Development Center, Fu Jen Catholic University, Taipei, Taiwan
[4]Department of Food Nutrition and Health Biotechnology, College of Medical and Health Science, Asia University, Taichung, Taiwan
[5]Big Data Center, Lo-Hsu Medical Foundation, Lotung Poh-Ai Hospital, Yilan, Taiwan
[6]Division of Radiation Oncology, Lo-Hsu Medical Foundation, Lotung Poh-Ai Hospital, Yilan, Taiwan
[7]Department of Healthcare Administration, College of Medical and Health Science, Asia University, Taichung, Taiwan
[8]Cancer Center, Lo-Hsu Medical Foundation, Lotung Poh-Ai Hospital, Yilan, Taiwan
[9]Centers for Regional Anesthesia and Pain Medicine, Taipei Municipal Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan
[10]Department of Management, College of Management, Fo Guang University, Yilan, Taiwan
[11]College of Medical and Health Science, Asia University, Taichung, Taiwan
[12]Attending Physician, Division of Radiation Oncology, Department of Medicine, Lo-Hsu Medical Foundation, LotungPoh-Ai Hospital, No.83, Nangchang St., Luodong Township, Yilan County 265, Yilan, Taiwan
[13]Institute of Electrophysiology, Henan Academy of Innovations in Medical Science, Zhengzhou, China

Received: 28 February 2024 / Accepted: 24 February 2025
Published online: 15 March 2025

References

1. Janssen TL, Alberts AR, Hooft L, Mattace-Raso F, 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.
2. Inouye SK. Delirium in older persons. N Engl J Med. 2006;354(11):1157–65.
3. Bilimoria KY, Liu Y, Paruch JL, Zhou L, Kmiecik TE, Ko CY, Cohen ME. Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. J Am Coll Surg. 2013;217(5):833–42. e831-833.
4. Fong TG, Jones RN, Marcantonio ER, Tommet D, Gross AL, Habtemariam D, Schmitt E, Yap L, Inouye SK. Adverse outcomes after hospitalization and delirium in persons with alzheimer disease. Ann Intern Med. 2012;156(12):848–56. W296.
5. Seitz DP, Gill SS, Gruneir A, Austin PC, Anderson GM, Bell CM, Rochon PA. Effects of dementia on postoperative outcomes of older adults with hip fractures: a population-based study. J Am Med Dir Assoc. 2014;15(5):334–41.
6. Whitlock EL, Vannucci A, Avidan MS. Postoperative delirium. Minerva Anestesiol. 2011;77(4):448–56.
7. Yang Q, Wang J, Huang X, Xu Y, Zhang Y. Incidence and risk factors associated with postoperative delirium following primary elective total hip arthroplasty: a retrospective nationwide inpatient sample database study. BMC Psychiatry. 2020;20(1):343.
8. 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):418.
9. Park EA, Kim MY. Postoperative delirium is associated with negative outcomes and Long-Term mortality in elderly Koreans: A retrospective observational study. Med (Kaunas) 2019, 55(10).
10. Rosman M, Rachminov O, Segal O, Segal G. Prolonged patients' In-Hospital waiting period after discharge eligibility is associated with increased risk of infection, morbidity and mortality: a retrospective cohort analysis. BMC Health Serv Res. 2015;15:246.
11. Salomon B, Dasa V, Krause PC, Hall L, Chapple AG. Hospital length of stay is associated with increased likelihood for venous thromboembolism after total joint arthroplasty. Arthroplast Today. 2021;8:254–e257251.
12. Shi Z, Mei X, Li C, Chen Y, Zheng H, Wu Y, Zheng H, Liu L, Marcantonio ER, Xie Z, et al. Postoperative delirium is associated with Long-term decline in activities of daily living. Anesthesiology. 2019;131(3):492–500.
13. Smith PJ, Attix DK, Weldon BC, Monk TG. Depressive symptoms and risk of postoperative delirium. Am J Geriatr Psychiatry. 2016;24(3):232–8.
14. Robinson TN, Eiseman B. Postoperative delirium in the elderly: diagnosis and management. Clin Interv Aging. 2008;3(2):351–5.
15. Mart MF, Williams Roberson S, Salas B, Pandharipande PP, Ely EW. Prevention and management of delirium in the intensive care unit. Semin Respir Crit Care Med. 2021;42(1):112–26.
16. Beaupre LA, Jones CA, Saunders LD, Johnston DW, Buckingham J, Majumdar SR. Best practices for elderly hip fracture patients. A systematic overview of the evidence. J Gen Intern Med. 2005;20(11):1019–25.
17. Donovan AL, Braehler MR, Robinowitz DL, Lazar AA, Finlayson E, Rogers S, Douglas VC, Whitlock EL. Anesthesia resident quality improvement C: an Implementation-Effectiveness study of a perioperative delirium prevention initiative for older adults. Anesth Analg. 2020;131(6):1911–22.
18. Bui LN, Pham VP, Shirkey BA, Swan JT. Effect of delirium motoric subtypes on administrative Documentation of delirium in the surgical intensive care unit. J Clin Monit Comput. 2017;31(3):631–40.
19. la Cour KN, Andersen-Ranberg NC, Weihe S, Poulsen LM, Mortensen CB, Kjer CKW, Collet MO, Estrup S, Mathiesen O. Distribution of delirium motor subtypes in the intensive care unit: a systematic scoping review. Crit Care. 2022;26(1):53.
20. Chen TJ, Chung YW, Chang HR, Chen PY, Wu CR, Hsieh SH, Chiu HY. Diagnostic accuracy of the CAM-ICU and ICDSC in detecting intensive care unit delirium: A bivariate meta-analysis. Int J Nurs Stud. 2021;113:103782.
21. Boettger S, Breitbart W. Phenomenology of the subtypes of delirium: phenomenological differences between hyperactive and hypoactive delirium. Palliat Support Care. 2011;9(2):129–35.
22. Cavallazzi R, Saad M, Marik PE. Delirium in the ICU: an overview. Ann Intensive Care. 2012;2(1):49.
23. Raats JW, Steunenberg SL, de Lange DC, van der Laan L. Risk factors of postoperative delirium after elective vascular surgery in the elderly: A systematic review. Int J Surg. 2016;35:1–6.
24. Raats JW, van Eijsden WA, Crolla RM, Steyerberg EW, van der Laan L. Risk factors and outcomes for postoperative delirium after major surgery in elderly patients. PLoS ONE. 2015;10(8):e0136071.
25. Lee HB, Mears SC, Rosenberg PB, Leoutsakos JM, Gottschalk A, Sieber FE. Predisposing factors for postoperative delirium after hip fracture repair in individuals with and without dementia. J Am Geriatr Soc. 2011;59(12):2306–13.
26. Guo Y, Jia P, Zhang J, Wang X, Jiang H, Jiang W. Prevalence and risk factors of postoperative delirium in elderly hip fracture patients. J Int Med Res. 2016;44(2):317–27.
27. Yildizeli B, Ozyurtkan MO, Batirel HF, Kuscu K, Bekiroglu N, Yuksel M. Factors associated with postoperative delirium after thoracic surgery. Ann Thorac Surg. 2005;79(3):1004–9.
28. Kanno M, Doi M, Kubota K, Kanoya Y. Risk factors for postoperative delirium and subsyndromal delirium in older patients in the surgical ward: A prospective observational study. PLoS ONE. 2021;16(8):e0255607.
29. Cole MG, Primeau FJ. Prognosis of delirium in elderly hospital patients. CMAJ. 1993;149(1):41–6.
30. Robinson TN, Raeburn CD, Tran ZV, Angles EM, Brenner LA, Moss M. Postoperative delirium in the elderly: risk factors and outcomes. Ann Surg. 2009;249(1):173–8.

31. Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell FE Jr., Inouye SK, Bernard GR, Dittus RS. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA. 2004;291(14):1753–62.
32. McCusker J, Cole M, Abrahamowicz M, Primeau F, Belzile E. Delirium predicts 12-month mortality. Arch Intern Med. 2002;162(4):457–63.
33. 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(14):1657–62.
34. Kiely DK, Marcantonio ER, Inouye SK, Shaffer ML, Bergmann MA, Yang FM, Fearing MA, Jones RN. Persistent delirium predicts greater mortality. J Am Geriatr Soc. 2009;57(1):55–61.
35. Moskowitz EE, Overbey DM, Jones TS, Jones EL, Arcomano TR, Moore JT, Robinson TN. Post-operative delirium is associated with increased 5-year mortality. Am J Surg. 2017;214(6):1036–8.
36. Hamilton GM, Wheeler K, Di Michele J, Lalu MM, McIsaac DI. A systematic review and Meta-analysis examining the impact of incident postoperative delirium on mortality. Anesthesiology. 2017;127(1):78–88.
37. Gottschalk A, Hubbs J, Vikani AR, Gottschalk LB, Sieber FE. The impact of incident postoperative delirium on survival of elderly patients after surgery for hip fracture repair. Anesth Analg. 2015;121(5):1336–43.
38. Dubljanin Raspopovic E, Markovic Denic L, Marinkovic J, Radinovic K, Ilic N, Tomanovic Vujadinovic S, Kadija M. Early mortality after hip fracture: what matters? Psychogeriatrics. 2015;15(2):95–101.
39. Dubljanin-Raspopovic E, Markovic Denic L, Marinkovic J, Grajic M, Tomanovic Vujadinovic S, Bumbasirevic M. Use of early indicators in rehabilitation process to predict one-year mortality in elderly hip fracture patients. Hip Int. 2012;22(6):661–7.
40. Bai J, Liang Y, Zhang P, Liang X, He J, Wang J, Wang Y. Association between postoperative delirium and mortality in elderly patients undergoing hip fractures surgery: a meta-analysis. Osteoporos Int. 2020;31(2):317–26.
41. Zeng S, Chang CH, Sun M, Chen WM, Wu SY, Zhang J. Comparison of surgical complications after curative surgery in patients with oral cavity squamous cell carcinoma and sarcopenia. J Cachexia Sarcopenia Muscle. 2023;14(1):576–84.
42. Wu SY, Huang JY, Lai YR, Lin JA. Association between long-term opioid use and cancer risk in patients with chronic pain. Response to Br J Anaesth 2022; 129: e104-e105. Br J Anaesth 2023.
43. Sun M, Chen WM, Wu SY, Zhang J. Dementia risk amongst older adults with hip fracture receiving general anaesthesia or regional anaesthesia: a propensity-score-matched population-based cohort study. Br J Anaesth. 2023;130(3):305–13.
44. Sun M, Chen WM, Wu SY, Zhang J. Dementia risk after major elective surgery based on the route of anaesthesia: A propensity score-matched population-based cohort study. EClinicalMedicine. 2023;55:101727.
45. Sun M, Chen WM, Wu SY, Zhang J. Sarcopenia is associated with an increase in long-term use of analgesics after elective surgery under general anesthesia. Reg Anesth Pain Med. 2023;48(5):205–10.
46. Sun M, Lin JA, Chang CL, Wu SY, Zhang J. Association between long-term opioid use and cancer risk in patients with chronic pain: a propensity score-matched cohort study. Br J Anaesth. 2022;129(1):84–91.
47. Sun M, Chang CL, Lu CY, Zhang J, Wu SY. Effect of opioids on cancer survival in patients with chronic pain: a propensity score-matched population-based cohort study. Br J Anaesth. 2022;128(4):708–17.
48. Nia A, Popp D, Thalmann G, Greiner F, Jeremic N, Rus R, Hajdu S, Widhalm HK. Predicting 30-Day and 180-Day mortality in elderly proximal hip fracture patients: evaluation of 4 risk prediction scores at a level I trauma center. Diagnostics (Basel) 2021, 11(3).
49. Sun M, Chen WM, Wu SY, Zhang J. Association between postoperative hyperactive delirium and major complications in elderly patients undergoing emergency hip fracture surgery: A large-scale cohort study. Geriatr Gerontol Int. 2024;24(7):730–6.
50. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat. 2011;10(2):150–61.
51. Austin PC. The performance of different propensity score methods for estimating marginal hazard ratios. Stat Med. 2013;32(16):2837–49.
52. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. Stat Med. 2015;34(28):3661–79.
53. Austin PC. The use of propensity score methods with survival or time-to-event outcomes: reporting measures of effect similar to those used in randomized experiments. Stat Med. 2014;33(7):1242–58.
54. Alagiakrishnan K, Wiens CA. An approach to drug induced delirium in the elderly. Postgrad Med J. 2004;80(945):388–93.
55. Caplan LR. Delirium: a neurologist's view–the neurology of agitation and overactivity. Rev Neurol Dis. 2010;7(4):111–8.
56. Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens). N Engl J Med. 2014;371(22):2109–13.
57. Hosker C, Ward D. Hypoactive delirium. BMJ 2017, 357j2047.
58. Lodewijckx E, Debain A, Lieten S, Bravenboer B, Mets T. Pharmacologic treatment for hypoactive delirium in adult patients: A brief report of the literature. J Am Med Dir Assoc. 2021;22(6):1313–e13161312.
59. Kuss O, Blettner M, Borgermann J. Propensity score: an alternative method of analyzing treatment effects. Dtsch Arztebl Int. 2016;113(35–36):597–603.
60. Schulte PJ, Mascha EJ. Propensity score methods: theory and practice for anesthesia research. Anesth Analg. 2018;127(4):1074–84.
61. Rubin DB, Thomas N. Matching using estimated propensity scores: relating theory to practice. Biometrics. 1996;52(1):249–64.
62. Elze MC, Gregson J, Baber U, Williamson E, Sartori S, Mehran R, Nichols M, Stone GW, Pocock SJ. Comparison of propensity score methods and covariate adjustment: evaluation in 4 cardiovascular studies. J Am Coll Cardiol. 2017;69(3):345–57.
63. Deb S, Austin PC, Tu JV, Ko DT, Mazer CD, Kiss A, Fremes SE. A review of Propensity-Score methods and their use in cardiovascular research. Can J Cardiol. 2016;32(2):259–65.
64. Cioci AC, Cioci AL, Mantero AMA, Parreco JP, Yeh DD, Rattan R. Advanced statistics: multiple logistic regression, Cox proportional hazards, and propensity scores. Surg Infect (Larchmt). 2021;22(6):604–10.
65. Sun M, Chen WM, Wu SY, Zhang J. The impact of postoperative agitated delirium on dementia in surgical patients. Brain Commun. 2024;6(2):fcae076.

Publisher's note