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ORIGINAL RESEARCH GERIATRIC ANESTHESIA

The relevance of preoperative frailty and postoperative delirium in elderly patients undergoing hip surgery

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ABSTRACT

Background & Objectives: Frailty status and delirium are common findings in the elderly in the perioperative period, and are associated with higher frequency of complications and poor outcomes after surgery. This study aimed to determine the rate and relationship between preoperative frailty and postoperative delirium (POD) in elderly people scheduled for hip surgery.

Methodology: A cross-sectional observational study was conducted on 104 elderly patients scheduled for hip surgery from October 2022 to November 2023 at the Centre for Anesthesia and Surgical Intensive Care, Bach Mai Hospital. The Modified Frailty Index (mFI) was used to assess the frailty. It includes 22 clinical and paraclinical variables and is useful to assess the preoperative frailty. We assessed postoperative delirium (POD) using the Confusion Assessment Method for the ICU (CAM-ICU) flow sheet during the first 4 days after surgery. Univariate and multivariate regression analyses were used to determine the association between frailty and delirium.

Results: A total of 104 patients were included in the analysis, and the proportion of patients with preoperative frailty (mFI ≥ 0.25) was 36.5%. Postoperative delirium occurred in 32 patients (30.8%). The frail patient group had a higher rate of postoperative delirium and a significantly longer average duration of delirium than the non-frail group (60.5% vs. 13.6% and 1.26 days vs. 0.35 days, respectively, P < 0.05). Multivariate regression analysis showed that mFI ≥ 0.25 was associated with POD status 4 days after surgery (aOR = 6.29; 95% CI = 1.43-27.6; P < 0.05).

Conclusions: The incidences of preoperative frailty and postoperative delirium in elderly patients undergoing elective hip surgery were 36.5% and 30.8%, respectively. Preoperative frailty is an independent risk factor for increased postoperative delirium.

Abbreviations: ADLs - Activities of Daily Living, NMS - New Mobility Score; ASA - American Society of Anesthesiologists, POD - Post-Operative Delirium; mFI - modified Frailty Index

Keywords: Postoperative delirium; Preoperative frailty; Hip fracture surgery; Elderly patient

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1. INTRODUCTION

Frailty is a non-specific condition, characterized by a decline in physiological reserves in the elderly, leading to increased vulnerability and reduced resistance to stressors, including anesthesia and surgery[1]. Generally, frailty is determined through criteria assessing the patient's comorbidities and ability to perform activities of daily living ADL).[1,2] Postoperative delirium (POD) is an acute and temporary brain dysfunction characterized by a decline in alertness and consciousness. POD is

associated with impairment of cognitive functions such as attention, memory, orientation, language, and perception (awareness). Regarding the cause, the majority of authors claim that POD is influenced by various factors, including both unchangeable factors (such as age, type of surgery) and changeable factors (such as anesthetic drugs, nutritional state, fragility, time of surgery, etc.).[3,4]

The literature reports a rate of frailty ranging from 15% to 60%, which is more common in elderly patients and those undergoing cardiovascular, orthopedic, and gastrointestinal surgery, depending on the diagnostic criteria, patient population, and type of surgery.[1,5] While POD has a rate ranging from 10–80%, especially in recovery rooms, surgical intensive care units, and surgical wards, POD complications are also more common in the elderly, especially in patients having cardiac surgery and orthopedic surgery.[6-8] Previous studies have shown that patients with preoperative frailty and/or POD tend to experience poor clinical outcomes such as prolonged hospital stays, increased incidence of postoperative complications (such as infection, impaired consciousness, etc.), an increased rate of hospital readmissions, increased medical costs, and even higher mortality than patients without these conditions.[1,3,9,10]

Hip surgery is quite common in the elderly. The main reason for needing surgery is fractures of the hip joint, which is related to degeneration of the bones and joints. It is estimated that the number of hip fractures will increase from 1.12 million in 2018 to 2.56 million in 2050 in Asia.[11] This is also the type of surgery with the highest rate of POD complications among non-cardiac surgeries.[6,8] In order to ensure that patients are receiving the best preventative and therapeutic measures possible during the perioperative period, it is crucial to identify and screen for preoperative frailty as well as risk factors for POD. This will reduce the likelihood of complications and enhance surgical outcomes. Some studies have demonstrated a correlation between preoperative frailty and the development of delirium following specific surgeries.[12-14] We carried out this study to assess the incidence of preoperative frailty, the prevalence of POD, and the correlation between these two conditions in elderly patients scheduled for hip surgery in our population.

2. METHODOLOGY

2.1 Study design

The prospective observational study was conducted at the Centre for Anesthesia and Surgical Intensive Care, Bach Mai Hospital, from October 2022 to November 2023. The Ethics Committee at Bach Mai hospital approved the research protocol under Decision No. 4670/QĐ-BM. The preoperative anesthesia examination involved explaining and signing the patient's consent to participate. The study complied with the principles of the Helsinki Declaration on ethical issues in biomedical research.

The study included all patients scheduled for hip arthroplasty who were 60 y of age or older. Exclusion criteria included patients identified as having mental illnesses, preoperative severe cognitive disorders, alcohol abuse, being unable to complete the CAM-ICU test after surgery, or having severe complications during the perioperative period such as shock, coma, or death.

Anesthetic management and routine monitoring, such as electrocardiography, non-invasive blood pressure measurement, and pulse oximetry, were performed. We monitored blood pressure, heart rate, and blood oxygen saturation every 3 min. Did not use premedication for patients. The anesthetic method was spinal anesthesia or general anesthesia, chosen depending on the patient's condition, surgical requirements, and the patient's wishes. Fluid infusion, use of vasoconstrictors, control of body temperature, and hemodynamics were performed as usual. Variables related to the characteristics of patients, anesthesia, surgery, and delirium assessment were assessed and recorded. Figure 1 presents the study flowchart.

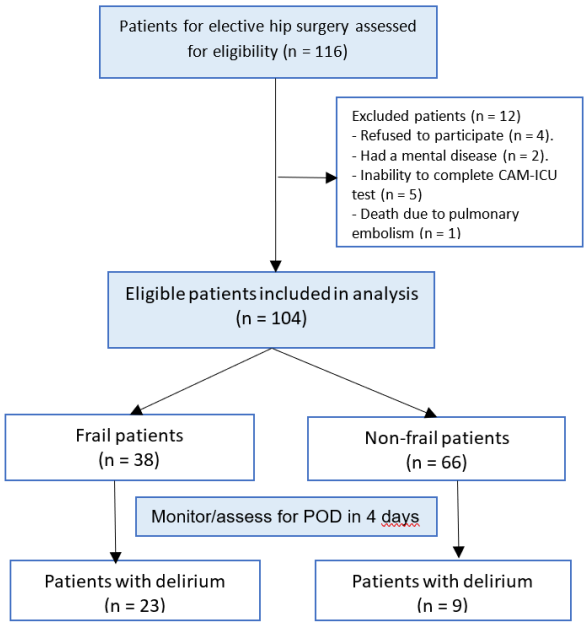

Figure 1: Flowchart of study

2.2. Frailty assessment

Frailty assessment and screening tools were assessed[1,2] to be suitable for orthopedic trauma patients. In this study we used a modified frailty index (mFI) consisting

Table 1: Perioperative characteristics according to frailty

Variables	Full sample (n=104)	mFI ≥ 0.25 (n = 38)	mFI < 0.25 (n = 66)	P-value
Demographic characteristics				
Age				
≤ 70	35 (33.7%)	3 (7.9%)	32 (48.5%)	< 0.01
71-80	35 (33.7%)	14 (36.8%)	21 (31.8%)	
> 80	34 (32.7%)	21 (55.2%)	13 (38.2%)	
Female	65 (62.5%)	29 (76.3%)	36 (54.5%)	0.027
General clinical characteristics				
Underweight	20 (19.2%)	15 (39.4%)	5 (7.6%)	< 0.001
Healthy	44 (42%)	17 (44.7%)	27 (40.9%)	
Overweight/obesity	40 (38.5%)	6 (15.8%)	34 (51.5%)	
Unintentional weight loss	15 (14.4%)	11 (28.9%)	4 (6.1%)	0.001
ASA classification				
II	65 (62.5%)	14 (36.8%)	51 (77.2%)	< 0.001
III/ IV	39 (37.5%)	24 (63.1%)	15 (22.7%)	
Physical status before a fracture				
ADL = 1	48 (46.2%)	24 (63.2%)	24 (36.4%)	0.008
NMS = 1	46 (44.2%)	25 (65.8%)	21 (31.8%)	0.001
Comorbid disease				
< 3 disease	76 (73.1%)	10 (26.3%)	66 (100%)	< 0.001
≥ 3 disease	28 (26.9%)	28 (73.7%)	0	
Abnormal test values				
Hypoalbuminemia	27 (26%)	18 (47.4%)	9 (13.6%)	< 0.001
Low hematocrit levels	52 (50%)	30 (78.9%)	22 (33.3%	< 0.001
Type of surgery				
Partial hip replacement	38 (36.5%)	13 (34.2%)	25 (37.8%)	>0.25
Total hip replacement	40 (38.5%)	15 (39.5%)	25 (37.8%)	
Osteosynthesis	26 (25%)	10 (26.3%)	16 (25.4%)	
Anesthesia				
Regional anesthesia	77 (74%)	30 (78.9%)	47 (71.2%)	0.124
General anesthesia	27 (26%)	8 (21.1%)	19 (28.8%)	
Delirium assessment				
Incidence of delirium	32 (30.8%)	23(60.5%)	9 (13.6%)	< 0.001
Mean time delirium (days)	0.68 ± 1.16	1.26 ±1.39	0.35 ± 1.02	< 0.01

(mFI: modified Frailty Index; ADL: Activities of Daily Living; NMS: New Mobility Score, ASA: ASA Physical Status Classification)

of 22 criteria; including 17 criteria for the comorbidities, two criteria assessing the ability to perform daily activities before the fracture (ADL and NMS), one criterion related to weight loss, and 2 paraclinical criteria (Appendix 1. Data collection sheet). A trained anesthesiologist performed a frailty screening the day before surgery. Each criterion received a score of either 0 or 1, with a maximum total score of 22 points and a minimum score of 0. We calculated the mFI by dividing the patient's score by 22. In this study, frailty was defined as mFI ≥ 0.25; patients in the non-frail group would have an mFI < 0.25; and those in the frail group would have

an mFI ≥ 0.25. (Refer to Gandossi's study[9] using 21 criteria with a cut-off point of 0.25 to determine frailty).

2.3. Diagnosis of postoperative delirium

In this study, CAM-ICU was the tool of choice to evaluate and diagnose postoperative delirium.[4] The CAM-ICU assessment includes four steps: (1) acute change or fluctuating mental status; (2) decreased attention; (3) disorienting thinking; and (4) altered mental status. Anesthesiologists, trained to assess delirium using the CAM-ICU, performed the evaluation. Anesthesiologists diagnosed a patient with delirium when they observed both features (1) and (2), as well as either feature (3) or (4). We assessed delirium twice daily, at 7:00 a.m. and 18:00 p.m., in the first four days following surgery. This assessment method, according to Hassan et al., can detect up to 97% of delirium cases.[7]

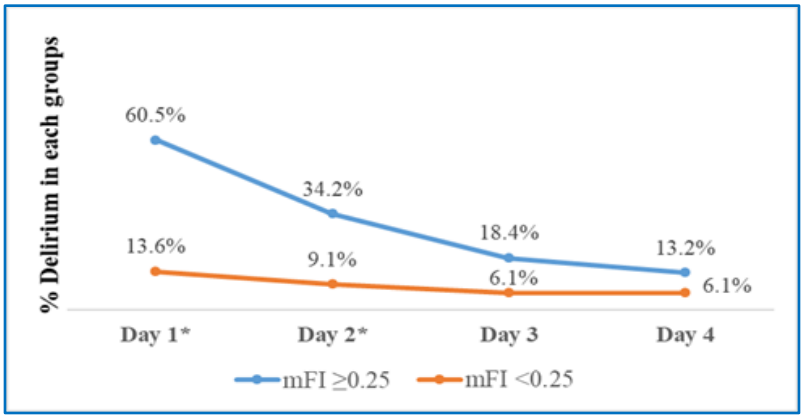

Figure 2: The incidence of POD in each group during 4 postoperative days (* P < 0.05)

2.4. Statistical analysis

The data were processed and analyzed using Stata 13.1 software. We calculated and included in the analysis the distribution of clinical characteristics, frailty rates, and postoperative delirium rates in the general population and in the frail and non-frail groups. We present qualitative variables as frequencies and percentages, and quantitative variables as the mean, standard deviation, minimum value, and maximum value.

The normal distribution of this variables was assessed by Kolmogorov–Smirnov test. Comparison between two groups for quantitative variables used the Mann-Whitney test if distribution was not normal, and unpaired test for normal distribution. For qualitative variables, we used the χ^2 test or Fisher's exact test. A $P < 0.05$ was considered statistically significant. Factors affecting POD were determined using a univariate regression model ($P < 0.05$, and the 95% CI does not contain the value 0). We then performed a multivariable logistic regression analysis, using frailty status as the regressor, and adjusted for identified associated factors. The association between frailty and POD was expressed through an aOR with $P < 0.05$ and a 95% CI not containing a value of 0 considered significant.

3. RESULTS

We assessed 116 patients scheduled for elective hip surgery. Among them, 4 patients refused to participate, 2 patients had a mental disease, 5 patients were unable to complete the CAM-ICU test, and 1 patient died due to pulmonary embolism. Then, we had 104 eligible patients left for inclusion in the analysis. Table 1 presents the demographic, clinical, and some frailty-related characteristics. The mean age was 75.1 ± 9.1 y (varying from 60 to 95 y), in which the female gender accounted for 62.5%, and the average BMI was 21.4 ± 3.0 (varying from 15.8 to 28.7) kg/m². There was no statistically significant difference in the type of surgery and anesthesia method in the frail and non-frail groups ($P > 0.05$).

There were 38 patients (36.5%) with frailty (with an mFI level ≥ 0.25); 14.4% had unintentional weight loss; and 37.5% of patients had an ASA classification > II. The proportion of patients with ADL and NMS scores equal to 1 was 46.2% and 44.2%, respectively; 27% of patients had at least 3 co-morbidities. The two most common diseases were arthritis (63.5%) and diabetes (26.9%). Hypoalbuminemia and low hematocrit had rates of 27% and 50%, respectively. These characteristics had a significantly higher distribution in the mFI ≥ 0.25 group than in the mFI < 0.25 group ($P < 0.05$). (Table 1).

The proportion of patients with POD within four days after surgery was 30.8%. All POD cases appeared within the first 24 h and decreased over the next three days. The POD rate in the frail group was significantly higher than the non-frail group on days 1 and 2 (Figure 2). The proportion of patients with prolonged delirium (≥ 2 days) in the frail group was also significantly higher than in the non-frail group. The average number of delirium days in the frail group was 1.26, significantly higher than the non-frail group, which was 0.35 ($P < 0.05$) (Table 1).

Univariate regression analysis results confirm variables related to POD rate, including age, gender, ASA classification, surgical method, anesthetic method, and frailty status ($P < 0.05$). We found that frailty is an independent risk factor for POD, using a multivariate regression analysis model with frailty status as the regressor and related factors taken into account. People

Table 2: Variables associated with delirium and their multivariable logistics regression analysis

Delirium		Univariable analysis OR (95% CI)	Multivariable analysis aOR (95% CI)
Frailty	Yes	1	1
	No	9.71 (3.73-25.31) *	6.29 (1.43-27.60) *
Age group (y)	< 70	1	1
	70-80	1.78 (0.52-6.10)	0.72 (0.11-4.59)
	> 80	7.60 (2.37-24.34) *	2.16 (0.33-13.96)
Sex	Male	1	1
	Female	3.67 (1.35-9.98) *	2.45 (0.57-10.53)
ASA	II	1	1
	III & IV	5.73 (2.32-14.14) *	2.81 (0.69-11.29)
Type of surgery	Total hip replacement	1	1
	Partial hip replacement	6.60 (2.14-20.36) *	6.12 (1.19-31.30)
	Osteosynthesis	2.43 (0.68-8.74)	2.30 (0.37-14.22)
Anesthesia	Regional	1	1
	General	7.02 (2.68-18.41) *	5.47 (1.51-19.82)

(P < 0.05; OR: Odds Ratio; aOR: adjusted Odds Ratio; CI: Confidence Interval)*

who were frail had a 6.29 times higher rate of delirium than people who were not frail (aOR = 6.29; 95% CI = 1.43–27.60, P < 0.05) (Table 2).

4. DISCUSSION

In our study, the proportion of patients with frailty was 36.5%. In patient populations undergoing hip surgery, this rate varies between studies due to the use of different frailty assessment tools. Kristler reported a frailty rate of 51% (using the frailty phenotype with 5 clinical criteria).[10] Gandossi reported a frailty rate of 36.4% (using a modified Frailty Index with 21 criteria).[9] In Feng's study, 48% of patients had preoperative frailty when assessed by the Frailty Index, which included 40 deficit variables.[15] Rebecca used a 32-criteria assessment tool on 8640 patients with hip surgery. Rebecca classified the patients as non-frail, vulnerable, and frail. The results showed that the rate of frailty was 22.7%, and the rate of vulnerability was 32.9%.[16]

A meta-analysis of 15 studies involving 3250 adult surgical patients recently confirmed the association between preoperative frailty and POD. The results showed that the preoperative frailty rate was 27.1% and the POD rate was 15.8%. This analysis confirmed that frailty is associated with a significantly increased risk of POD.[17] In the patient population 65 y of age and older, another meta-analysis by Gracie et al., including 9 studies of 945 patients undergoing elective surgery, found frailty rates ranging from 18.6% to 56%, and frail patients had a higher risk of POD than non-frail patients (OR = 2.14 and a 95% CI of 1.43–3.19).[14]

We conducted research on patients undergoing hip surgery; this is one of the types of surgery with the highest rate of POD. The findings revealed a 30.8% incidence of POD, with a close correlation between preoperative frailty status and an increased risk of POD. The POD rate in the frail group was much higher than the non-frail group (60.5% vs. 13.6%). Multivariable regression analysis showed that frailty was an independent risk factor for POD, with the likelihood of POD occurring in the frail group being 6.29 times higher than in the non-frail group (aOR = 6.29; 95% CI = 1.43-27.6; P < 0.05). Our findings are also consistent with the results of several recent studies on orthopedic surgery patients. Feng identified 48.0% of the 148 older patients with hip fractures as preoperatively frail and 52.0% as non-frail in his study. The incidence of POD on day 7 was 24.3% (36/148), and preoperative frailty was associated with a significantly higher risk of POD compared with no frailty (42.3% vs. 7.8%, P < 0.001).[15] Shooka Esmaeeli et al. retrospectively studied 556 elderly people having orthopedic surgery and found that preoperative frailty significantly increased the risk of POD (OR 1.33; 95% CI 1.02–1.72, P = 0.03). In this study, the POD rate was 14% when using CAM to evaluate delirium within 24 h after surgery.[13] Yun Chen reported a POD rate of 17.2% in a prospective study of 383 patients undergoing total joint arthroplasty and identified frailty status as an independent predictor of POD occurrence (OR, 3.31; 95% CI, 1.91–5.72; P =

0.008). In this study, frailty was confirmed based on 11 criteria, and delirium was assessed using the Diagnostic and Statistical Manual of Mental Disorders (DSM-V).[18]

Differences in rates as well as the degree of association between studies may be due to differences in patient characteristics, frailty and delirium assessment criteria, duration, and timing of delirium assessment. Despite this, results from studies consistently show that frailty is an independent risk factor for POD. Although the pathogenesis of frailty and delirium remains unclear, most authors believe that a multitude of factors plays a role. Several studies have linked frailty with reduced DNA repair capacity, mitochondrial dysfunction, increased free radical production, inflammation, innate immune dysfunction, disorders of metabolic and hormonal balances, and patients' psychological factors.[5] The mechanism of delirium is also thought to be related to neurotransmitters, inflammatory responses, stress, disorders of blood supply, and metabolism in the brain.[3] The association between frailty and delirium may lie in the common pathogenesis of these two conditions.[19]

5. LIMITATIONS

As with similar studies, this study also has some limitations. First, the study's sample size is not really large and cannot completely rule out the presence of many covariates, which may lead to residual bias and affect the results. Second, this study used the mFI to match a group of orthopedic patients; however, because it only divides patients into frailty and non-frailty groups, accurately assessing the impact of different levels of frailty on POD is challenging. Besides, the choice of a cut-off of mFI 0.25 to determine frailty does not really have clear evidence. Finally, a study lasting 4 days after surgery may not be enough to detect all cases of POD. On the contrary, due to the long duration of delirium assessment after surgery, confounding factors related to postoperative management may appear. Besides, some factors that can affect the occurrence of POD, such as blood loss, hemodynamic instability, hypoxemia, and drugs used in the perioperative period, have not been considered.

6. CONCLUSION

Our study shows that the incidences of preoperative frailty and postoperative delirium in elderly patients undergoing elective hip surgery were 36.5% and 30.8%, respectively. Preoperative frailty is an independent risk factor for increased postoperative delirium (aOR=6.29; 95% CI=1.43-27.6; $P < 0.05$). Therefore, we maintain the belief that interventions should be implemented whenever possible in order to screen for and optimize frailty and prevent delirium during the perioperative period.

7. Data availability

The numerical data generated during this research is available with the authors.

8. Acknowledgement

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9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors' contribution

All authors took part in the concept, literature search, conduct of the study and manuscript preparation.

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Appendix 1. Data collection sheet (Frailty index scoring system)				
1. Pre-fracture ADL score				
SELF-CARE ACTIVITIES				
Dressing	0 = No problems 1 = Independent, but slow or clumsy 2 = Wrong sequence, forgets items 3 = Needs help with dressing 9 = Don't know			
TRAVEL				
Public Transportation	0 = Uses public transportation as usual 1 = Uses public transportation less frequently 2 = Has gotten lost using public transportation 3 = No longer uses public transportation 9 = Never used public transportation regularly or don't know			
SHOPPING AND MONEY				
Food shopping	0 = No problem 1 = Forgets items or buys unnecessary items 2 = Needs to be accompanied while shopping 3 = No longer does the shopping 9 = Never had responsibility in this activity or don't know			
Total score ≥ 3 then ADLs = 1 point; else, ADLs = 0 point				
2. New mobility score (NMS)				
Mobility	Not at all (0)	With help from another person (1)	With an aid (2)	No difficulty (3)
Able to get about the house				
Able to get out of the house				
Able to go shopping				
Total score ≤ 7 then MNS = 0 point; else NMS = 1 point				
3. Comorbids			Not present (0)	Present (1)
Atrial fibrillation				
Pre-fracture dementia				
Myocardial infarction				
Congestive heart failure				
Severe liver disease				
Kidney failure				
Cancer				
Metastasis				
Leukaemia or lymphoma				
Peripheral arterial disease				
Cerebral vascular disease				
Stroke				
Parkinson's disease				
Diabetes				
Chronic lung disease				
Gastric ulcer				
Rheumatic disease				
Hypoabuminemia (< 35g/dL)				
Low hemoglobin levels (< 120 g/dL for female and < 130 g/dL for male):				
Unintentional weight loss (more than 5% in the last year)				
Total points				
Frailty index (total points divide by 22)				
ADL: Activities of Daily Living; NMS: New Mobility Score				

