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Frailty and Postoperative Delirium in Elderly Patients Undergoing Elective Surgery: An Analytical Study

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ABSTRACT

Introduction

Postoperative delirium (POD) in geriatric patients significantly increases morbidity and mortality. Frailty predisposes patients to significant adverse postoperative outcomes. This study evaluates the occurrence of preoperative frailty using Edmonton Frail Scale (EFS) and its association with postoperative delirium in elderly patients.

Methods

An analytical cohort study was conducted among patients aged ≥ 65 undergoing elective non-cardiac surgery. Preoperative frailty, cognitive reserve and comorbidities were assessed with validated tools. Intraoperative variables including anesthesia type, surgery, surgical duration, intraoperative complications including hypotension were recorded. Postoperative delirium was assessed twice daily for 72 hours postoperatively using confusion assessment method (CAM). Unadjusted and multivariable logistic regression analyses were performed to identify independent risk factor and evaluate the association between frailty and delirium after adjusting for relevant covariates.

Results

The occurrence of delirium was 9.70%(16/165). Preoperative frailty was present in 55 (33.33%) participants. Postoperative delirium was seen in 43.33% of moderate to severe frail group compared to 0.91% in the non-frail group ($p < 0.001$). In the multivariable analysis, after adjustment for age and intraoperative hypotension, the odds of postoperative delirium increased about twofold for every one-point increase in Edmonton Frail Scale score (aOR 2.20; 95% CI 1.57-3.50, $p < 0.001$). Intraoperative hypotension was another significant factor (aOR 12.88; 95% CI 2.66-77.58, $p < 0.002$).

Conclusion

The preoperative frailty score and intraoperative hypotension were significant predictors of postoperative delirium. Implementing routine frailty screening and hemodynamic stability in frail elderly population are essential strategies to decrease the risk of postoperative delirium.

Keywords

Delirium; frailty; geriatrics; hypotension; postoperative

INTRODUCTION

As life expectancy rises due to medical advancements, a greater percentage of the elderly population seeks surgery. These patients are susceptible to postoperative delirium (POD). POD is independently associated with increased morbidity and mortality.[1] Recent evidence suggests frailty, a state characterized by reduced physiological reserve is a good predictor of POD.[2] Edmonton Frail Scale (EFS)[3], a globally validated tool for screening frailty and a high score has higher odds of occurrence of POD.[4] Its utility in Nepalese healthcare, however, is unexplored as most of the data originates from high-income countries. The knowledge gap exists, as we do not know the occurrence of frailty and its association with postoperative delirium in our population. The rationale for this study is to establish whether chronological age or frailty is associated with POD in our setting. This study aims to evaluate the occurrence of frailty and association between frailty severity and POD in elderly patients in a Nepalese tertiary care center.

METHODS

A prospective observational cohort study was conducted at Kathmandu Medical College Teaching Hospital from July 2025 to December 2025. Ethical approval was obtained from institutional review committee reference no. 25052025/11. Written informed consent was obtained from all participants or their representatives before the enrollment. All patients aged more than 65 years presenting for elective non-cardiac surgery were considered for inclusion. Patients were excluded if they had a preexisting diagnosis of dementia or cognitive impairment, or were lost to follow-up before completing 72-hour postoperative assessment.

Sample size was calculated based on an estimated POD prevalence of 12.5% derived from a comparable study in elderly patients.[5] Using the formula for a single proportion, $Z_{1-\alpha/2}^{2}P(1-p) \,/\, d^{2}$, where $Z_{1-\alpha/2}=$ Standard normal variate at 5% type 1 error. P is prevalence and d is margin of error, a total of 165 participants were required.

The preoperative assessment was conducted in the preoperative room. The frailty was assessed by EFS (0–17), a validated tool scored from 0 to 17, with higher scores indicating greater frailty. Participants were categorized into not Frail (EFS 0-5), mildly frail (EFS 6–7) and moderate severely frail (EFS ≥8). Baseline cognitive reserve was measured via the Mini-Cog (scored 0–5), a validated screening tool for cognitive impairment.[6] Comorbidity burden was measured with Charlson Comorbidity Index (CCI).[7] Trained investigators associated with the study performed these assessments.

Intraoperative variables were recorded, which included type of anesthesia (general, neuraxial block or peripheral nerve block), surgical category, duration of surgery. Intraoperative hypotension (IOH) was defined as mean arterial pressure (MAP) below 65 mmHg sustained for more than 5 minutes measured by non-invasive blood pressure monitoring device with readings taken every two minutes when hypotension was detected, or by invasive blood pressure monitoring depending on the surgery or clinical indication. Blood loss exceeding 500 milliliters was recorded.

POD was assessed twice daily morning and evening for 72 hours postoperatively using the Confusion Assessment Method (CAM), which is a validated diagnostic algorithm with high sensitivity and specificity for delirium.[8] Anesthesiologists or critical care specialist well versed in the CAM scoring system made the assessments. A positive POD diagnosis was made in any patient who met CAM criteria on at least one assessment within 72-hour window.

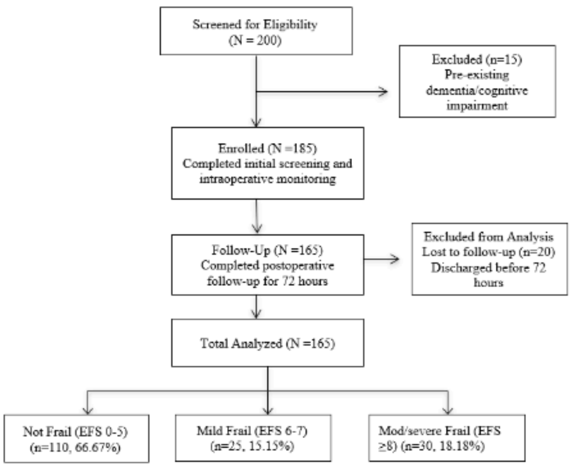

Figure 1. STROBE flow chart

Data were entered and analyzed using R studio (version 2024.4.2.764). Continuous variables are reported as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate to distribution. Categorical variables are reported as frequencies and percentages. Continuous variables were compared using ANOVA, and categorical variables were compared using Chi-squared or Fisher's Exact test as appropriate. Unadjusted logistic regression was used to determine association between each predictor and POD. Multivariable Logistic regression was performed to evaluate the association between frailty and delirium after adjusting for relevant covariates. Odds Ratios (OR) and 95% Confidence Intervals (CI) were calculated. A p-value <0.05 was considered statistically significant.

RESULTS

The study included 165 elderly participants with a median age of 69 years (IQR 66-76), of whom 101 (61.21%) were male and 64 (38.79%) were female.

Based on the EFS score, occurrence of frailty was seen in 55(33.33%) of our study population. Among these, 30(18.18%) were classified as moderately to severely frail. Out of 165 participants, 16(9.70%) developed postoperative delirium. The occurrence of POD was significantly high in moderate severely frail 13(43.33%) compared to 1(0.91%) in the non-frail group (p <0.001). Baseline and surgical characteristics, stratified by frailty category are tabulated in Table1.

Frailty category was significantly associated with surgical category, with higher proportions of moderately-to-severely frail patients undergoing hip 9(30.00%) and 10(33.33%) major abdominal procedures compared to other categories (p=0.002).

Table 1. Baseline characteristics and surgical variables by frailty status

Variable	Not Frail n=110 n(%)	Mid-Frail n=25 n(%)	Mod/Severe Frail n=30 n(%)	Overall N=165 n(%)	P-value
Delirium (No)	109(99.09%)	23(92.00%)	17(56.67%)	149(90.30%)	<0.001
Delirium (Yes)	1(0.91%)	2(8.00%)	13(43.33%)	16(9.70%)	
Age(IQR) years	67(65-70)	71(68-76)	76.50(71-82)	69(66-76)	<0.001
Gender (male)	70(64.20%)	14(56%)	17(56.70%)	101(61.21%)	0.845
Gender (female)	40(36.40%)	11(44%)	13(43.30%)	64(38.79%)	
Charlson comorbidity Index (Mean±SD)	3.17±0.90	4.48±0.77	4.30±1.44	3.58±1.15	<0.001
Surgery Duration (hours) median(range)	1.00(0.40-5.00)	1.00(0.35-5.00)	1.50(0.48-4.00)	1.00(0.35-5.00)	0.29
Anesthesia: General anaesthesia	45(40.91%)	10(40%)	3(10%)	58 (35.15%)	0.124
Anaesthesia: Neuraxial block	49(44.50%)	11(44%)	21(70%)	81(49.10%)	
Anesthesia: Nerve block	16(14.60%)	4(16%)	6(20%)	26(15.80%)	
Hypotension	6(5.45%)	4(16%)	9(30%)	19(11.52%)	0.012
Blood loss (>500ml)	3(2.73%)	1(4%)	3(10%)	7(4.24%)	

An unadjusted logistic regression analysis was performed to compare the characteristics of patients who developed post-operative delirium (POD) versus those who did not is presented in table 2. EFS score was significantly higher in delirium group compared to non-delirium (8.9±2.6 vs. 4.9±2.8, p< 0.001). Unadjusted logistic regression analysis showed that frailty score, age and intraoperative hypotension were significantly associated with POD.

Table 2. Unadjusted logistic regression analysis of preoperative and intraoperative factors associated with POD

Predictor Variable	Crude Odds Ratio (cOR)	95% Confidence Interval	P-value
Edmonton Frail Scale (Continuous)	2.38	1.74 – 3.60	<0.001
Age (per year increase)	1.10	1.03 – 1.17	0.005
Gender (Male vs. Female)	0.59	0.21 – 1.72	0.337
CCI Score (Continuous)	1.52	0.96 – 2.47	0.078
Surgery Duration (per hour)	1.22	0.75 – 1.85	0.353
Hypotension (Yes vs. No)	17.87	5.60 – 60.73	<0.001
Neuraxial block	4.40	1.12 – 29.19	0.06

A multivariable logistic regression model was constructed to examine the association between frailty and POD after adjusting for age and intraoperative hypotension, as shown in Table 3. This multivariable table confirms that the severity of frailty has positive association for postoperative delirium (POD). This indicates that frailty represented by EFS score has strong positive association with POD, as every one point increase in the EFS score, the odds of developing POD increased significantly (aOR 2.20; CI 1.57-3.50, p <0.001). Intraoperative hypotension also has positive strong association with POD, while age lost its statistical significance once frailty was included (p= 0.278).

Table 3. Multivariate Logistic Regression Analysis for Post-Operative Delirium

Predictor Variable	Adjusted Odds Ratio (aOR)	95% Confidence Interval	P-value
Edmonton Frail Scale (Continuous)	2.20	1.57 – 3.50	<0.001
Intraoperative Hypotension	12.88	2.66- 77.58	0.002

Predictor Variable	Adjusted Odds Ratio (aOR)	95% Confidence Interval	P-value
Age	1.07	0.94-1.21	0.278

DISCUSSION

This prospective observational cohort study demonstrates that preoperative frailty, assessed by Edmonton Frail Scale (EFS), and intraoperative hypotension are independent risk factors of postoperative delirium in elderly patients undergoing elective non-cardiac surgery. Notably, important data such as the chronological age lost statistical significance as an independent risk factor once frailty was accounted for. This suggests that frailty may account for some of the vulnerability usually attributed to age. These findings extend the evidence, which are predominantly from high-income countries to a low middle-income country (LMIC).

The occurrence of frailty in our geriatric population was significant 55(33.33%). This is consistent with global estimates of LMIC, where nutritional deficit and late presentation often accelerate biological aging.[9] The prevalence of frailty measured by different tools in different cohorts has reported to be from 10 to 34.9%.[10] The three-category distribution of frailty in our cohort with 30(18.18%) classified as moderately-to-severely frail reflects a population with high vulnerability at baseline.

The overall occurrence of POD was 9.70%, which is at the lower end for non-cardiac surgery. The reported rates of postoperative delirium ranges from 0.7% to 50% depending on population characteristics, surgical category and assessment methods.[11] Our relatively low estimate reflects several factors, namely the exclusion of emergency cases, the exclusion of patients with preexisting dementia, twice daily rather than continuous assessment of CAM, these factors essentially is a protocol limitation may have lead to under detection of hypoactive or brief delirium episodes.

Patients who developed delirium had significantly higher mean EFS scores compared to those who did not (8.9±2.6 vs. 4.9±2.8,p<0.001). In our multivariable analysis, EFS was treated as a continuous variable, to avoid loss of statistical information associated with categorization. This approach allowed the assessment of gradient risk between frailty severity and delirium. Each one-point increase in the EFS was associated with nearly a two-fold increase in the odds of postoperative delirium (adjusted OR = 2.20, p < 0.001) after adjusting for other covariates. Even in a meta-analysis, the association of preoperative frailty with POD was significant with pooled odds ratio was 2.47 in non cardiac surgeries.[12] The odds are higher in patients undergoing cardiac surgery, where authors have claimed a higher odds of 5 and 6.31 of developing delirium.[13,14]

The gradient across the frailty categories provides more information that just overall incidence of POD. The data suggests POD occurred in 1(0.91%) of non-frail participants, 2(8%) of mildly frail and 13(43.33%) of moderate-to-severe frail participants. This dose response type association pattern is a significant finding in our study. It aligns with the conclusion of Schindele and colleagues' systemic review and meta-analysis which characterizes frailty severity as a gradient risk.[10] It is also consistent with Ehrlich et al, who reported progressively increasing POD incidence across frailty category in a mixed surgical cohort.[15] Knowledge about severity of frailty and its significant relation between various risk factors will help us plan and decrease the risk of POD. POD is a preventable serious complication in the perioperative period. POD is associated with increased risk of mortality, hospitalization, long-term cognitive decline and dementia.[11]

In the unadjusted analysis, age was significantly associated with increased delirium (cOR 1.10; 95% CI 1.03-1.17, p = 0.005) and had a higher comorbidity burden (mean CCI 4.2±1.4 vs. 3.5±1.1, p=0.025). This therefore demonstrates that higher the age, comorbidity burden and frailty higher the incidence of POD. Our data resonates with studies conducted in similar surgical population.[4,15,16] This finding is consistent with literatures which argues about shift from chronological to biological age as an essential factor for surgical outcome and patient counseling.[17] In our multivariable model, chronological age was not an independent risk factor of POD once EFS was included (aOR 1.07, 95% CI 0.94-1.21, p = 0.278). While age remains a demographic risk factor, it is an imprecise estimate of physiological reserve that determines vulnerability to surgical stress. The EFS, incorporates functional dependence, cognitive status, comorbidity burden, social support along with physical indicators which provides objective categorization of the frailty status. Therefore, frailty screening prior to elective surgery allows identification of high-risk patients, who may benefit from rehabilitation, optimized anesthesia plan, enhanced monitoring and early postoperative delirium protocols-regardless of their age in years.

Intraoperative hypotension (IOH) was our second independent risk factor of POD in our cohort, with an adjusted odds ratio of 12.88 (95% CI 2.66-77.58). We acknowledge the width of the confidence interval suggest a degree of imprecision, this is likely due to the small event size and the lower value remains above one, indicating a strong direction of association. The evidence on IOH as a predictor of POD has been a debated topic, a recent meta-analysis by Yin and colleagues reported a pooled relative risk of 1.89 and an odds ratio of 2.48 for the association between intraoperative hypotension and POD across the surgical population.[18]

There seems to be a biological plausibility to event of IOH leading to the cause that is POD. Maintaining cerebral oxygenation and perfusion are highly critical in elderly patients, particularly in those with high frailty scores. When these falls below the critical levels cerebral auto regulation failure may occur, which then leads to neuronal ischemia and activate neuro-inflammatory response to surgical stress. The additive effect of frailty and hypotension observed in our study, likely stems from activated microglia that is present in certain phenotypes. In the aging brain where resident immune cells are hyperactive, intraoperative hypotension, triggers a catastrophic neuro-inflammatory cascade, further disrupting blood-brain barrier (BBB) and accelerating neural network dysfunction.[19] Whether frailty and IOH act additively on increasing the risk of POD is an important question that stems from our study and hence should be explored in future studies. Evidence supports individualized blood pressure targets and cerebral oxygenation monitoring is beneficial in these high-risk patients. [20,21]

A 2024 update by European Society of Anesthesia and Intensive Care highlights the association between preexisting vulnerabilities and acute physiological stressors as pathogenesis of POD.[22] As evidenced by Leung et al, postoperative patients who developed delirium had a higher level of neurodegeneration markers.[23] Furthermore, there has been studies citing excessive release of proinflammatory cytokines like interleukin IL-1β, IL-6, IL-8, IL-10, CRP and tumor necrosis factor -α (TNF-α) in the perioperative period. These cytokines penetrate BBB and trigger microglial activation that initiates neuro-inflammation. [23,24]

Our study found no significant association between anesthesia type and POD; this finding mirrors the recommendation by American Society of Anesthesiologist advisory task force, which suggests no superiority with either technique in reducing POD. Although regional anesthesia was more frequent employed in patients with higher EFS scores. This is likely a selection bias, as regional anesthesia is chosen more often than general anesthesia in a frail patient whenever possible by the attending anesthesiologist. However our data show that choice of anesthesia doesn't mitigate the risk if the underlying frailty and intraoperative hypotension are present.

To our knowledge, this is the first study in Nepalese tertiary care setting to specifically investigate the interplay between frailty, intraoperative hypotension and POD in elderly surgical population. In our healthcare system, growing geriatric surgical population with resource constrains, precludes us from complex biomarker-based risk stratification. Under these circumstances, tools used in the study like EFS, Mini-cog, CCI and CAM are all validated, freely available and require no special equipment. Our findings are highly implementable across various resource-limited settings.

Our findings supports two clinical strategies, one is routine screening for frailty in the preoperative period to identify high risk patients and second is to maintain intraoperative hemodynamic vigilance with a target MAP above 65 mmHg in elderly frail patients. Both of these interventions are highly effective yet easily applicable and their combined application has the potential to reduce the burden of a preventable and serious postoperative complication.

There are several limitations in this study. The study was conducted at a single center and the results may not reflect generalizability to rural Nepal. We did not measure specific biomarkers (eg. IL-6, CRP,) to correlate with EFS score. Additionally, our postoperative assessment was limited to 72 hours window. While the majority of POD manifests within this time frame, late onset POD could have been missed. Adding on, while we adjusted for several key covariates in our study, there remain unmeasured confounding factors such as electrolyte imbalances, dosage of opioids. Finally, the incidence of delirium may be higher in emergency surgeries, which we excluded.

CONCLUSION

Preoperative frailty, as measured by EFS and intraoperative hypotension are the primary independent risk factors of postoperative delirium in elderly population undergoing non-cardiac surgery. This study demonstrates that frailty severity, rather than age is an important risk factor for postoperative delirium, these results provide clear framework for preoperative risk stratification. Standardized frailty screening and intraoperative blood pressure management are low cost and high impact pathways to improve geriatric surgical outcome.

CONFLICT OF INTEREST

None

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AUTHORS' CONTRIBUTION

Mona Sharma: concept, design, definition of intellectual content, literature search, data acquisition, manuscript preparation, editing and review;

Sushil Poudel: design, definition of intellectual content, literature search, manuscript editing and review;

Saurya Dhungel: Design, literature search, statistical analysis, manuscript editing and review;

Abiya Pradhan: Design, data acquisition, manuscript review;

Bijay KC: Design, data collection, manuscript review.

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