Correlation Analysis Between Preoperative Platelet-to-Albumin Ratio and Postoperative New-Onset Frailty in Elderly Patients Undergoing Elective Surgery: A Multicenter Study Postprint

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Abstract

Background Frailty is an age-related syndrome. Current assessment of frailty primarily relies on single inflammatory factors or nutritional indicators, lacking systematic diagnostic markers. Chronic inflammation and nutritional status constitute part of the pathophysiological mechanisms of frailty, and platelet count and nutritional status are easily obtainable. However, studies on the correlation between mixed inflammatory markers combining platelet count and nutritional status and frailty are scarce.

Objective To investigate the correlation between preoperative platelet count/albumin ratio (PAR) and new-onset frailty at 7 days postoperatively in elderly patients undergoing elective surgery.

Methods This study was a secondary analysis based on the dataset of the Elderly Perioperative Adverse Events Prediction Model Construction Study (EPAE), using a cross-sectional survey method. Elderly patients hospitalized and scheduled for elective surgery were selected from 7 hospitals including the Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Shunde Hospital of Guangzhou University of Chinese Medicine, Fourth Clinical Medical College of Guangzhou University of Chinese Medicine, Foshan Hospital of Traditional Chinese Medicine, Huizhou Hospital of Traditional Chinese Medicine, Zhongshan Hospital of Traditional Chinese Medicine, and Dongguan Hospital of Guangzhou University of Chinese Medicine between February and October 2023. A total of 2,035 patients without preoperative frailty were included. At 7 days postoperatively, patients were divided into a non-frailty

group (1,691 cases) and a new-onset frailty group (344 cases) according to the diagnostic criteria of the Chinese version of the Frail scale. General data and perioperative factors influencing frailty were collected and compared between the two groups. Multivariate Logistic regression analysis was used to evaluate correlations between variables. PAR was divided into 4 levels according to quartiles: Q1 (PAR$ 4.160), $Q2(PAR$: 4.161 5.339), $Q3(PAR$: 5.340 6.479), $Q4(PAR$ $6.480). Multivariate Logistic regression analysis with multiple models was performed to evaluate the impact of different PAR levels on frailty. The incidence of new-onset frailty at 7 days postoperatively in different age groups was analyzed, and receiver operating characteristic (ROC) curves were plotted to calculate the area under the curve (AUC) and optimal cutoff value to evaluate the predictive value of preoperative PAR for new-onset frailty at 7 days postoperatively in elderly patients.

Results There were statistically significant differences between the two groups in age, caregivers, sedentary behavior, weekly aerobic exercise duration, weekly resistance training duration, proportion of stress history, Age-Adjusted Charlson Comorbidity Index (ACCI) score, Athens Insomnia Scale (AIS) score, Patient Health Questionnaire-9 (PHQ-9) score, Social Support Rating Scale (SSRS) score, American Society of Anesthesiologists (ASA) classification, preemptive analgesia, anesthesia method, proportion of surgery types, operation time, and intraoperative blood transfusion (P<0.05). Moreover, PAR in the new-onset frailty group was significantly higher than that in the non-frailty group (P<0.001). Multivariate Logistic regression analysis showed that after adjusting for all confounding factors, high-level PAR was a risk factor for new-onset frailty at 7 days postoperatively in elderly patients (OR=1.22, 95%CI=1.16~1.29, P<0.001). The results of multivariate Logistic regression analysis for different PAR levels showed that after adjusting for all confounding factors, compared with Q1 level PAR, Q2, Q3, and Q4 level PAR were all risk factors for new-onset frailty at 7 days postoperatively in elderly patients, with Q4 level PAR having the highest risk (OR=6.06, 95%CI=3.90~9.41, P<0.001). Stratified analysis results showed that the incidence of new-onset frailty at 7 days postoperatively in different age groups increased significantly with elevated preoperative PAR (P<0.001). The AUC of preoperative PAR for predicting new-onset frailty at 7 days postoperatively in elderly patients was 0.635 (95%CI=0.606~0.665, P<0.001), with an optimal cutoff value of 4.345, sensitivity of 89.20%, and specificity of 31.20%.

Conclusion Preoperative PAR has certain predictive value for new-onset postoperative frailty in elderly patients, with higher PAR levels indicating greater risk of new-onset postoperative frailty.

Full Text

Preoperative Platelet-to-Albumin Ratio in Elective Geriatric Surgery Patients and Its Correlation with Postoperative Incidental Frailty: A Multicenter Study

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Abstract

Background: Frailty is an age-related syndrome characterized by reduced physiological reserve and diminished stress response across multiple organ systems, leading to increased risks of postoperative complications, prolonged hospitalization, readmission, and mortality. Current frailty assessment relies primarily on single inflammatory markers or nutritional indicators, lacking systematic diagnostic biomarkers. Chronic inflammation and nutritional status are integral to the pathophysiology of frailty, while platelet count and albumin levels are simple and readily accessible clinical parameters. However, few studies have examined the association between composite inflammatory markers combining platelet count and nutritional status with frailty.

Objective: To investigate the correlation between preoperative platelet-to-albumin ratio (PAR) and new-onset frailty at 7 days postoperatively in elderly patients undergoing elective surgery.

Methods: This secondary analysis utilized data from the Early Warning Model Construction Study of Perioperative Adverse Events for elderly patients (EPAE). Using a cross-sectional survey design, we enrolled elderly patients hospitalized for elective surgery at seven hospitals: the Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Shunde Hospital of Guangzhou University of Chinese Medicine, the Fourth Clinical Medical College of Guangzhou University of Chinese Medicine, Foshan Hospital of Chinese Medicine, Huizhou Hospital of Chinese Medicine, Zhongshan Hospital of Chinese Medicine, and Dongguan Hospital of Guangzhou University of Chinese Medicine, between February and October 2023. A total of 2,035 patients without preoperative frailty were included and divided into a non-frailty group (1,691 patients) and a new-onset frailty group (344 patients) based on the Chinese version of the Frail Scale assessed at 7 days postoperatively. General patient characteristics and perioperative frailty risk factors were collected and compared between groups. Multifactorial logistic regression analysis was performed to assess variable associations. PAR was stratified into quartiles: Q1 (PAR $\leq$ 4.160), Q2 (PAR: 4.161–5.339), Q3 (PAR: 5.340–6.479), and Q4 (PAR $\geq$ 6.480). Multi-model multifactorial logistic regression analysis evaluated the impact of different PAR levels on frailty. Stratified analysis by age group was conducted, and receiver operating characteristic (ROC) curves were plotted to calculate the area under the curve (AUC) and optimal cutoff value for assessing the predictive value of preoperative PAR for postoperative new-onset frailty.

Results: Significant differences between groups were observed in age, caregiver status, sedentary behavior, weekly aerobic exercise duration, weekly resistance training duration, stress history proportion, age-corrected Charlson Comorbidity Index (ACCI) score, Athens Insomnia Scale (AIS) score, Patient Health Questionnaire-9 (PHQ-9) score, Social Support Rating Scale (SSRS) score, American Society of Anesthesiologists (ASA) classification, preemptive analgesia, anesthesia method, surgery type proportions, operative time, and intraoperative transfusion volume (all $P < 0.05$). PAR was significantly higher in the new-onset frailty group compared to the non-frailty group ($P < 0.001$). Multifactorial logistic regression revealed that elevated PAR was an independent risk factor for new-onset frailty at 7 days postoperatively after adjusting for all confounders (OR = 1.22, 95% CI = 1.16–1.29, $P < 0.001$). When PAR was analyzed as a categorical variable, Q2, Q3, and Q4 levels were all associated with increased risk compared to Q1, with Q4 showing the highest risk (OR = 6.06, 95% CI = 3.90–9.41, $P < 0.001$). Stratified analysis demonstrated that the incidence of postoperative new-onset frailty increased significantly with higher preoperative PAR in both age groups ($P < 0.001$). The AUC for preoperative PAR in predicting new-onset frailty was 0.635 (95% CI = 0.606–0.665, $P < 0.001$), with an optimal cutoff value of 4.345, sensitivity of 89.20%, and specificity of 31.20%.

Conclusion: Preoperative PAR demonstrates predictive value for postoperative new-onset frailty in elderly patients, with higher PAR levels indicating greater risk. PAR may serve as a valuable biomarker for perioperative frailty

risk assessment in geriatric surgical patients.

Keywords: Frailty; Platelet count; Albumin; Platelet-to-albumin ratio; Elderly patients; Postoperative frailty

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1.1 Study Participants

The Early Warning Model Construction Study of Perioperative Adverse Events for elderly patients (EPAE) is a multicenter investigation designed to identify and predict the risk of adverse events in geriatric patients undergoing elective surgery, thereby providing safer and more effective medical care. Using convenience sampling, the EPAE study enrolled elderly patients from seven hospitals between February and October 2023: the Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Shunde Hospital of Guangzhou University of Chinese Medicine, the Fourth Clinical Medical College of Guangzhou University of Chinese Medicine, Foshan Hospital of Chinese Medicine, Huizhou Hospital of Chinese Medicine, Zhongshan Hospital of Chinese Medicine, and Dongguan Hospital of Guangzhou University of Chinese Medicine.

In this secondary analysis of the EPAE dataset, we initially included 2,678 elderly patients. After excluding 299 patients who underwent diagnostic procedures only and 344 patients with pre-existing frailty, 2,035 patients were included in the final analysis. Inclusion criteria were: (1) age 60–85 years; (2) scheduled for elective surgery; (3) American Society of Anesthesiologists (ASA) classification I–III; and (4) provision of informed consent. Exclusion criteria included: (1) visual or severe hearing impairment, or cognitive dysfunction preventing completion of assessments; (2) malignant tumors or organ failure; and (3) psychiatric disorders. The study protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Guangzhou University of Chinese Medicine (BE2022-165-01), and all patients provided written informed consent. The trial was registered with the Chinese Clinical Trial Registry (ChiCTR2300071535). This study adheres to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines to ensure comprehensive and transparent reporting.

1.2 Methods

1.2.1 General Data Collection: Demographic information included gender, age, body mass index (BMI), marital status, smoking and alcohol consumption, education level, monthly household income per capita, pre-retirement occupation, caregiver status, fruit intake frequency, sedentary behavior, weekly aerobic exercise duration, and weekly resistance training duration.

1.2.2 Assessment of Perioperative Frailty Risk Factors: Disease-related factors included polypharmacy, stress history, Age-adjusted Charlson Comorbidity Index (ACCI) score, Nutritional Risk Screening 2002 (NRS2002) score,

Instrumental Activities of Daily Living (IADL) scale score, Athens Insomnia Scale (AIS) score, Numerical Rating Scale (NRS) for pain, and Mini-Cognitive Assessment (Mini-Cog) score. Psychosocial factors comprised Social Support Rating Scale (SSRS) score and Patient Health Questionnaire-9 (PHQ-9) score. Surgical factors encompassed ASA classification, surgical site, preemptive analgesia, operative time, intraoperative transfusion volume, anesthesia method, and surgery type.

1.2.3 Inflammatory Marker Assessment: Preoperative blood samples were obtained within three days before surgery, with the sample collected closest to the surgical date retrieved from electronic medical records. Complete blood count results were used to calculate platelet-to-lymphocyte ratio (PLR), product of platelet and neutrophil count (PPN), systemic immune-inflammation index (SII), and platelet-to-albumin ratio (PAR). Blood samples were collected in the morning after overnight fasting.

1.2.4 Frailty Assessment: Frailty was evaluated using the Frail Scale, which assesses five domains: fatigue, endurance, mobility, comorbidity, and unintentional weight loss in the past year, with total scores ranging from 0 to 5. A score of $ $3 indicates frailty. Based on the 7-day postoperative assessment, patients were categorized into the non-frailty group (score 0–2) or new-onset frailty group (score 3–5).

1.3 Quality Control

All research team members underwent systematic training and used standardized scripts to explain the study purpose and questionnaire instructions. Strict inclusion and exclusion criteria were applied, and participation was strictly voluntary with informed consent. Trained investigators conducted one-on-one interviews and immediately reviewed completed questionnaires for accuracy, correcting any issues on-site. General demographic, disease-related, and psychosocial data were collected on admission day, along with the initial Frail Scale assessment. Surgical variables were recorded on the day of operation, and the Frail Scale was re-administered at 7 days postoperatively. All data were collected through standardized questionnaires, medical record review, and face-to-face interviews in compliance with ethical standards.

1.4 Statistical Analysis

All analyses were performed using SPSS version 27.0. Continuous variables with normal or approximately normal distribution were expressed as mean ± standard deviation and compared using independent samples t-test for two groups or one-way ANOVA for multiple groups, with LSD test for post-hoc pairwise comparisons. Non-normally distributed continuous variables were presented as median (P25, P75) and compared using Mann-Whitney U test for two groups or Kruskal-Wallis test for multiple groups. Categorical variables were expressed as frequency (percentage) and compared using chi-square test or Fisher' s ex-

act test. Multifactorial logistic regression analysis was used to assess variable associations. To control for confounding factors, we constructed four progressively adjusted logistic regression models, incorporating variables significant in univariate analysis and those clinically relevant to frailty risk assessment. PAR was analyzed both as a continuous variable and as quartiles (Q1: PAR $\leq$ 4.160; Q2: 4.161–5.339; Q3: 5.340–6.479; Q4: $\geq$ 6.480). Multi-model multifactorial logistic regression evaluated the effect of different PAR levels on frailty. Age-stratified analyses were performed, and ROC curves were generated to calculate AUC and optimal cutoff values for PAR' s predictive performance. Missing continuous variables were handled using multiple imputation or mean replacement when imputation was not feasible; missing categorical variables were addressed using logistic regression. A two-sided significance level of $\alpha = 0.05$ was set, with $P < 0.05$ considered statistically significant.

2.1 Comparison of General Characteristics Between Groups

Among the 2,035 enrolled patients, 344 (16.9%) developed new-onset frailty at 7 days postoperatively. Significant differences between the non-frailty and new-onset frailty groups were observed in age, caregiver status, sedentary behavior, weekly aerobic exercise duration, and weekly resistance training duration (all $P < 0.05$). No significant differences were found in gender, BMI, marital status, smoking, alcohol consumption, education level, monthly household income per capita, pre-retirement occupation, or fruit intake frequency (all $P > 0.05$) .

2.2 Comparison of Disease-Related and Psychosocial Variables

The new-onset frailty group exhibited higher proportions of stress history, ACCI scores, AIS scores, and PHQ-9 scores, along with lower SSRS scores, compared to the non-frailty group (all $P < 0.05$). No significant differences were observed between groups in polypharmacy proportion, NRS2002 score, IADL score, NRS pain score, or Mini-Cog score (all $P > 0.05$) .

2.3 Comparison of Surgery-Related Variables

The new-onset frailty group had significantly higher proportions of ASA class III, preemptive analgesia use, intravenous anesthesia, and minimally invasive surgery, along with longer operative times and greater intraoperative transfusion volumes, compared to the non-frailty group (all $P < 0.05$). No significant difference was found in surgical site between groups ($P > 0.05$) .

2.4 Comparison of Inflammatory Markers

PAR levels were significantly higher in the new-onset frailty group compared to the non-frailty group ($P < 0.001$). No significant differences were observed between groups in PLR, PPN, or SII (all $P > 0.05$) .

2.5 Multifactorial Logistic Regression Analysis of PAR and Postoperative Frailty

Using postoperative frailty at 7 days as the dependent variable, we performed multifactorial logistic regression analysis with PAR and covariates including age, caregiver status, sedentary behavior, weekly aerobic exercise duration, weekly resistance training duration, stress history, ACCI score, AIS score, SSRS score, PHQ-9 score, ASA classification, preemptive analgesia, operative time, intraoperative transfusion volume, anesthesia method, and surgery type as independent variables . Without adjustment, PAR level was significantly associated with new-onset frailty (OR = 1.19, 95% CI = 1.14-1.26, $P < 0.001$). After adjusting for all confounders, elevated PAR remained an independent risk factor (OR = 1.22, 95% CI = 1.16-1.29, $P < 0.001$). When PAR was analyzed as quartiles, Q2, Q3, and Q4 levels were all associated with increased risk compared to Q1 after full adjustment, with Q4 showing the highest risk (OR = 6.06, 95% CI = 3.90-9.41, $P < 0.001$) .

2.6 Age-Stratified Analysis of Postoperative Frailty

Stratified analysis by age groups (60-69 years and $ 70 $years) revealed that the incidence of new-onset frailty at 7 days postoperatively increased significantly with ascending PAR quartiles (Q1 to Q4) in both ages
trend = 31.634 and 34.878, respectively, both $P < 0.001$) .

2.7 ROC Curve Analysis of PAR for Predicting Postoperative Frailty

The ROC curve for preoperative PAR in predicting new-onset frailty at 7 days postoperatively yielded an AUC of 0.635 (95% CI = 0.606-0.665, $P < 0.001$). The optimal cutoff value was 4.345, with a sensitivity of 89.20% and specificity of 31.20% [Figure 1: see original paper].

Frailty is a prevalent syndrome among older adults that significantly impacts health outcomes. Surgical intervention, as a traumatic event, triggers stress responses that substantially increase the risk of postoperative frailty in elderly patients. Our study found that 16.9% (344/2,035) of geriatric surgical patients developed new-onset frailty at 7 days postoperatively. This incidence is lower than the 20.93%-80.67% range reported in previous studies, likely due to several factors. First, our cohort primarily comprised patients undergoing fracture surgery, whereas other studies focused on cancer patients who experience hypermetabolic states and negative energy balance that promote physical frailty. Second, 65.9% (1,342/2,035) of our patients underwent minimally invasive surgery, which is associated with less trauma, faster recovery, reduced postoperative pain, shorter hospital stays, and fewer complications compared to open surgery. Third, the timing of frailty assessment may influence results; for instance, one study evaluating frailty at 3 days postoperatively reported a 68.2% incidence, whereas our 7-day assessment may have allowed for initial recovery from acute surgical stress. Finally, different assessment tools yield

varying frailty rates, such as 59.0% using the Tilburg Frailty Indicator in gastrointestinal cancer patients versus 50% using the Short Physical Performance Battery in lung transplant recipients. Despite these methodological differences, the overall high incidence of postoperative frailty in older adults underscores the importance of our multicenter design in providing robust evidence for clinical risk assessment.

PAR, as a novel composite inflammatory marker integrating platelet count and nutritional status, correlates with the development and progression of various malignancies and inflammatory diseases and serves as a prognostic biomarker. Elevated PAR is associated with decreased overall and disease-free survival in cholangiocarcinoma and represents an independent risk factor for end-stage kidney disease. Our findings align with these observations, demonstrating that high PAR is an independent risk factor for new-onset frailty after surgery, with higher preoperative PAR values indicating greater postoperative frailty risk. This association is biologically plausible: elevated platelet counts reflect heightened inflammatory responses, while low albumin levels indicate malnutrition. Platelets mediate inflammation through adhesion to vascular walls at surgical sites, releasing pro-inflammatory cytokines such as CXCL1, CXCL4, and CXCL5. Activated platelets also induce vascular smooth muscle cells to release interleukin-1β, which promotes IL-6 and IL-8 production. These cytokines stimulate neutrophil production and pro-inflammatory mediator synthesis, creating a chronic inflammatory state that contributes to frailty development. Concurrently, albumin possesses anti-inflammatory, antioxidant, and anti-platelet aggregation properties. Hypoalbuminemia is a strong prognostic marker in cardiovascular disease, reflecting the severity of malnutrition-inflammation syndrome. Studies show that each 1 g/dL decrease in albumin is associated with a 0.4-point increase in frailty scores. Thus, the combination of elevated platelets and low albumin captured by PAR provides a robust indicator of frailty risk, supporting our conclusion that high preoperative PAR predicts postoperative frailty.

Our ROC analysis demonstrated that PAR predicts postoperative frailty with moderate discriminative ability (AUC = 0.635). The optimal cutoff of 4.345 yielded high sensitivity (89.20%) but low specificity (31.20%), suggesting PAR may be more useful for screening than definitive diagnosis. Notably, age-stratified analysis revealed that among patients aged $ $70 years, the frailty rate in the highest PAR quartile (Q4) reached 30.54%, nearly 3.6 times higher than the lowest quartile (8.37%). This strong dose-response relationship reinforces PAR' s utility as a risk stratification tool across age groups. The Chinese Expert Consensus on Frailty Prevention in Older Adults (2022) identifies disease status and nutritional condition as modifiable frailty risk factors amenable to early intervention. PAR, as a combined inflammatory-nutritional marker, offers clinicians a practical tool for identifying high-risk patients. Our findings suggest that routine preoperative PAR assessment could guide targeted interventions, including enhanced nutritional support, exercise programs, and inflammatory management strategies, to mitigate postoperative frailty and promote healthy aging.

Limitations and Future Directions

This multicenter study provides robust evidence for PAR' s predictive value, yet several limitations warrant consideration. First, the gender distribution was imbalanced, and unmeasured confounders such as chronic medication use, postoperative early mobilization, nutritional support, and complication management may have influenced results. Future studies should incorporate these variables into multivariate models. Second, despite excluding major comorbidities, occult platelet-related disorders may have residual confounding effects; more stringent exclusion criteria and subgroup validation are needed to confirm PAR' s independent association with postoperative frailty. Third, frailty was assessed only at 7 days postoperatively, limiting evaluation of long-term outcomes. Future research should include extended follow-up to assess PAR' s predictive value for long-term prognosis, quality of life, readmission rates, and mortality.

In conclusion, PAR, as an easily obtainable composite marker of inflammation and nutritional status, demonstrates predictive value for new-onset frailty in elderly surgical patients. Higher preoperative PAR levels indicate greater postoperative frailty risk, establishing PAR as a valuable biomarker for perioperative risk assessment in geriatric populations.

Author Contributions

CHENG Yuxin contributed to study conception, design, feasibility analysis, and manuscript drafting. CHENG Yuxin and WANG Zhiling performed data collection, table and figure preparation. FANG Jiamin and LIANG Hao conducted study evaluation and manuscript revision. WEI Lin was responsible for quality control, overall article supervision, and project management. LIAO Huilian, XU Mingming, CHEN Yumei, LI Yanfen, DONG Lijuan, and GUO Yingui contributed to multicenter data collection.

This article has no conflicts of interest to declare.

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Note: Figure translations are in progress. See original paper for figures.