The Association Between Preoperative Anxiety and Pain Severity, Opioid Requirement, Neutrophil-to-Lymphocyte Ratio, and Postoperative Blood Glucose After Gynecologic Laparotomy at Ngoerah Hospital

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Abstract

Background:
We assessed whether preoperative anxiety is associated with postoperative pain severity, opioid requirement, neutrophil-to-lymphocyte ratio (NLR), and blood glucose after gynecologic laparotomy.

Methods:
Prospective cohort at Ngoerah Hospital (May to June 2025). Anxiety was measured preoperatively with APAIS and categorized as non-anxious, mild, moderate, or severe. Outcomes were NRS pain at 6, 12, and 24 hours, total fentanyl in the first 24 hours, and NLR and blood glucose at 6 hours postoperatively. Multivariable analysis used MANCOVA (99% confidence intervals).

Result:
Fifty-four patients were included (mean age 41.78 ± 10.58 years). Anxiety distribution was 46.3% non-anxious, 25.9% mild, 24.1% moderate, and 3.7% severe. Higher anxiety was associated with higher NRS at 6 hours (B 0.842; 99% CI 0.475 to 1.209; p < 0.001), 12 hours (B 0.381; 0.247 to 0.515; p < 0.001), and 24 hours (B 0.158; 0.048 to 0.269; p = 0.048). Anxiety was associated with higher 24-hour fentanyl requirement (B 147.8 microg; 99% CI 124.062 to 171.651; p < 0.001), higher postoperative NLR (B 4.31; 99% CI 0.609 to 8.027; p = 0.024), and higher postoperative blood glucose (B 19.4 mg/dL; 99% CI 7.912 to 30.912; p = 0.001).

Conclusions:
Higher preoperative anxiety was independently associated with worse pain, greater opioid requirement, and higher postoperative NLR and blood glucose after gynecologic laparotomy.

Introduction

Preoperative anxiety is a frequent and clinically meaningful condition in surgical patients.[1] A systematic review and meta-analysis reported a pooled global prevalence of about 48% among surgical patients, showing that nearly one in two patients may experience significant anxiety before surgery.[2] In gynecologic laparotomy, anxiety is especially relevant because patients often anticipate major abdominal pain, anesthesia-related concerns, and potential impacts on reproductive health and recovery, which can amplify stress

responses and worsen the perioperative experience.[3,4]

Anxiety matters because it can alter pain perception and postoperative analgesic needs, potentially increasing opioid exposure. Acute postoperative pain remains common: studies in mixed surgical populations report a high burden of moderate-to-severe pain within the first 24 hours, and some data indicate that preoperative anxiety is associated with higher odds of moderate-to-severe postoperative pain.[5] For gynecologic laparotomy in particular, postoperative pain is often substantial and may drive higher opioid consumption, which is important because opioid escalation can increase risks such as nausea/vomiting, ileus, sedation, delayed mobilization, and prolonged length of stay.[6]

Perioperative anxiety-related stress responses may also be reflected in objective physiological markers relevant to postoperative monitoring. Postoperative hyperglycemia is not limited to patients with diabetes; it has been reported in around one-third of adult non-diabetic surgical patients (34.1%), and broader hospital data also describe hyperglycemia in a substantial proportion of general medicine and surgery patients.[7] Inflammatory shifts during surgical stress can also be captured by the neutrophil-to-lymphocyte ratio (NLR), which has been discussed as a practical marker of systemic inflammation and acute stress in surgical settings.[8–10] Therefore, this study aims to determine the relationship between preoperative anxiety and postoperative pain severity, opioid requirement, neutrophil-to-lymphocyte ratio, and blood glucose levels among patients undergoing gynecologic laparotomy at Ngoerah Hospital.

Material And Methods

Study design and setting

This prospective analytical observational study employed a cohort design to examine the association between preoperative anxiety and postoperative pain severity, opioid requirement, NLR, and blood glucose following gynecologic laparotomy. The study was conducted in the perioperative ward and the IBS operating theatre complex at Ngoerah Hospital, Denpasar, Bali, Indonesia, during May–June 2025. Consecutive eligible patients were enrolled using purposive sampling and followed from the preoperative assessment through the first 24 postoperative hours.

Participants

The target population comprised all patients scheduled for laparotomy at Ngoerah Hospital, and the accessible population included adults aged 18–65 years undergoing gynecologic laparotomy during the study period. Patients were eligible if they were aged 18–65 years, had a body mass index of 20–30 kg/m², had an American Society of Anesthesiologists (ASA) physical status I–III, and provided informed consent. Patients were excluded if they had a history of, or were currently using, psychiatric medications; were unable to communicate effectively; had diabetes mellitus; had chronic pain; or were taking systemic steroids routinely. Participants were considered dropouts if preoperative or postoperative measurements could not be completed (including missed or delayed assessments), if the procedure was cancelled or postponed, if clinical management changes precluded continued participation, if serious postoperative complications prevented further follow-up, if the patient withdrew consent, if an unstable medical condition prevented continuation, or if key data were incomplete for the main outcomes (anxiety, pain, opioid requirement, NLR, or blood glucose).

Exposure assessment: preoperative anxiety

Preoperative anxiety was assessed during the preoperative ward evaluation using the Amsterdam Preoperative Anxiety and Information Scale (APAIS). The APAIS comprises six items; the anxiety subscale is derived from items 1, 2, 4, and 5 (score range 4–20), while the information-need subscale is derived from items 3 and 6 (score range 2–10). Anxiety severity was interpreted using prespecified ranges: mild (5–8), moderate (9–14), and severe (15–20). For group comparisons, participants

were classified as non-anxious when the anxiety subscale score was 4 and anxious when the score was ≥5. Anxiety assessment was performed before any intraoperative period and, where applicable, before administration of anxiolytic premedication.

Outcomes

Pain intensity was measured using the Numeric Rating Scale (NRS), where 0 indicates no pain and 10 indicates the worst imaginable pain. NRS scores were recorded preoperatively and at 6, 12, and 24 hours postoperatively using the routine pain monitoring documentation. Opioid requirement was defined as the cumulative opioid administered during the first 24 postoperative hours and was recorded in fentanyl dose (µg) from clinical documentation, including opioid delivered via patient-controlled analgesia (PCA) and any additional opioid administered according to clinical need.

Inflammatory response was assessed using NLR, calculated by dividing the absolute neutrophil count by the absolute lymphocyte count from peripheral blood testing. NLR was obtained preoperatively and repeated at 6 hours postoperatively. Metabolic response was assessed using blood glucose measured preoperatively and at 6 hours postoperatively, either by capillary glucometer testing or laboratory analysis, and recorded in mg/dL. For NLR and blood glucose, both absolute postoperative values and the change from baseline to 6 hours were considered.

Perioperative management and data collection procedures

Participants fasted preoperatively according to hospital protocol, and fasting duration was recorded as a potential confounder. In the operating theatre, standard non-invasive monitoring was applied, including blood pressure measurement, electrocardiography, and pulse oximetry. Perioperative care followed routine institutional practice. Where indicated by clinical protocol, midazolam (0.05–0.1 mg/kg) could be administered as anxiolytic premedication. General anesthesia was induced with propofol (2–3 mg/kg), fentanyl (1–2 µg/kg), and a neuromuscular blocker (atracurium 0.5–0.6 mg/kg or rocuronium 0.6–1.0 mg/kg). Anesthesia was maintained with propofol or a volatile agent, consistent with routine practice, and additional analgesics could include opioid and non-opioid agents such as ketorolac; total intraoperative opioid and relevant analgesic adjuncts were recorded. Ondansetron 4 mg was administered for postoperative nausea and vomiting prophylaxis in accordance with local practice.

Postoperatively, IV PCA fentanyl was used for acute pain management. The PCA solution contained fentanyl 10 µg/mL, programmed to deliver a 25 µg bolus with an 8-minute lockout interval and a 4-hour limit of 100 µg. An Acute Pain Service (APS) team, not informed of the study details, documented PCA fentanyl consumption and NRS pain scores at 6, 12, and 24 hours postoperatively as part of routine care. Study investigators acted as observers and did not participate in clinical decision-making. Blood sampling or testing for NLR and glucose at 6 hours postoperatively was performed according to hospital procedures, and all study variables were entered into a predefined database for analysis.

Covariates

Prespecified potential confounders included age, educational attainment, occupation, marital status, ASA physical status, prior history of surgery/anesthesia, duration of preoperative fasting, operative duration, and total intraoperative opioid administered. These variables were obtained from patient interview and/or medical records.

Sample size

Sample size was estimated using a two-group comparison of means. Calculations based on opioid requirement assumed a standard deviation of 35 and a minimum clinically meaningful difference of 50, using one-sided parameters corresponding to $Z\alpha = 2.30$ and $Z\beta = 2.30$, resulting in approximately 21 participants per group. Calculations based on NLR assumed a standard deviation of 1.5 with a

minimum meaningful difference of 2, yielding approximately 24 participants per group; calculations based on blood glucose assumed a standard deviation of 30 with a minimum meaningful difference of 40, also yielding approximately 24 participants per group. The final target sample was set at 52 participants to ensure at least 24 participants per group after allowing for an anticipated 10% dropout rate.

Data analysis

Descriptive analyses were performed to summarize participant characteristics and study variables by anxiety group. Categorical variables were expressed as frequencies and percentages. Continuous variables were summarized as mean with standard deviation when normally distributed and as median with range when distributions were non-normal. Normality was assessed using the Shapiro–Wilk test and homogeneity of variance using Levene's test. Between-group comparisons for continuous outcomes were conducted using the independent t-test when assumptions were met, and the Mann–Whitney U test when distributions were non-normal. Proportions were compared using the chi-square test where appropriate. To evaluate the association between preoperative anxiety and key outcomes while accounting for covariates, multivariable analysis using a general linear model framework (MANCOVA) was planned, with results expressed as regression coefficients (B) and 99% confidence intervals; statistical significance was set at $p < 0.05$. All analyses were performed using SPSS version 26.0.

Result

Baseline characteristics

A total of 54 patients were included. The mean age was 41.78 ± 10.577 years (Table 1). Education levels were primary school 7 (13.0%), junior high school 5 (9.3%), senior high school 35 (64.8%), bachelor's degree 6 (11.1%), and master's degree 1 (1.9%) (Table 1). Most participants were homemakers (37; 68.5%), followed by private employee/self-employed (15; 27.8%) and civil servant (2; 3.7%) (Table 1). ASA physical status distribution was ASA I 18 (33.3%), ASA II 22 (40.7%), and ASA III 14 (25.9%) (Table 1). Prior anesthesia/surgery history was reported in 33 (61.1%) participants (Table 1). Median preoperative fasting duration was 11 hours (8–18), mean operative duration was 174.94 ± 43.563 minutes, and mean total intraoperative fentanyl was 287.04 ± 30.615 µg (Table 1). Intraoperative NSAID use was recorded in all participants (54; 100%) (Table 1).

Table 1. Baseline characteristics of the study sample (n = 54).

Characteristic	Value
Age, years (mean ± SD)	41.78 ± 10.577
Education, n (%)	
Primary school	7 (13.0)
Junior high school	5 (9.3)
Senior high school	35 (64.8)
Bachelor's degree	6 (11.1)
Master's degree	1 (1.9)
Occupation, n (%)	
Homemaker	37 (68.5)
Private employee / self-employed	15 (27.8)
Civil servant	2 (3.7)
ASA physical status, n (%)	
ASA I	18 (33.3)
ASA II	22 (40.7)
ASA III	14 (25.9)
Prior anesthesia/surgery history, n (%)	
Yes	33 (61.1)
No	21 (38.9)
Preoperative fasting duration, hours (median, min–max)	11 (8–18)
Operative duration, minutes (mean ± SD)	174.94 ± 43.563
Total intraoperative opioid (fentanyl), µg (mean ± SD)	287.04 ± 30.615
Intraoperative NSAID use, n (%)	54 (100)

Preoperative anxiety severity

Preoperative anxiety severity distribution was: non-anxious 25 (46.3%), mild anxiety 14 (25.9%), moderate anxiety 13 (24.1%), and severe anxiety 2 (3.7%) (Table 2).

Table 2. Distribution of preoperative anxiety severity.

Anxiety category	n (%)
Non-anxious	25 (46.3)
Mild anxiety	14 (25.9)
Moderate anxiety	13 (24.1)
Severe anxiety	2 (3.7)

Postoperative pain severity

Pain severity at 6, 12, and 24 hours after gynecologic laparotomy, stratified by preoperative anxiety category, is presented in Figure 2.

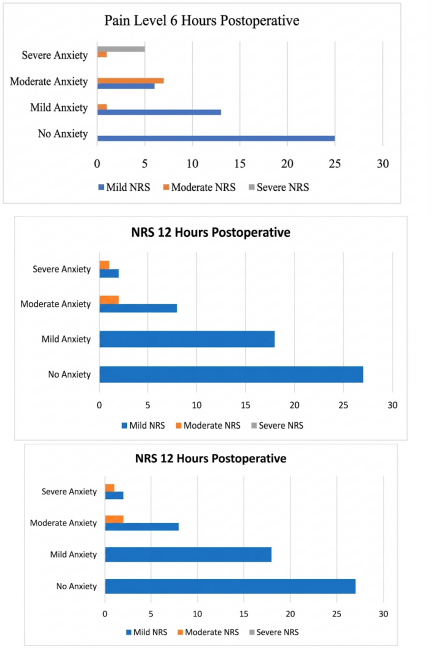

Figure 2. Pain Severity at 6, 12, and 24 Hours After Gynecologic Laparotomy.

Postoperative opioid requirement

Median postoperative fentanyl requirement in the first 24 hours was 352 µg (258–462) in the non-anxious group and 393 µg (265–500) in the mild anxiety group (Table 3). Median fentanyl requirement was 651 µg (426–731) in the moderate anxiety group and 757 µg (751–764) in the severe anxiety group (Table 3).

Table 3. Postoperative opioid requirement in the first 24 hours.

Anxiety category	Fentanyl, µg (median, min–max)
Non-anxious	352 (258–462)
Mild anxiety	393 (265–500)
Moderate anxiety	651 (426–731)
Severe anxiety	757 (751–764)

Neutrophil-to-lymphocyte ratio

Median preoperative NLR was 2.640 (0.9–6.6) in the non-anxious group, 2.21 (0.6–3.4) in the mild anxiety group, 3.04 (0.9–18.2) in the moderate anxiety group, and 3.515 (2.9–4.1) in the severe anxiety group (Table 4). Median postoperative NLR was 15.15 (6.4–22.2), 23.28 (7.6–48.4), 21.98 (13.5–63.6), and 17.650 (16.1–19.2) for the non-anxious, mild, moderate, and severe anxiety groups, respectively (Table 4).

Table 4. Neutrophil-to-lymphocyte ratio (NLR) preoperatively and postoperatively.

Anxiety category	Preoperative NLR (median, min–max)	Postoperative NLR (median, min–max)
Non-anxious	2.640 (0.9–6.6)	15.15 (6.4–22.2)
Mild anxiety	2.21 (0.6–3.4)	23.28 (7.6–48.4)
Moderate anxiety	3.04 (0.9–18.2)	21.98 (13.5–63.6)
Severe anxiety	3.515 (2.9–4.1)	17.650 (16.1–19.2)

Blood glucose

Median preoperative glucose was 90 mg/dL (78–136) in the non-anxious group, 92.5 mg/dL (66–111) in the mild anxiety group, 90 mg/dL (73–137) in the moderate anxiety group, and 110 mg/dL (102–118) in the severe anxiety group (Table 5). Median postoperative glucose was 142 mg/dL (118–248), 154.5 mg/dL (125–238), 178 mg/dL (133–242), and 223.5 mg/dL (211–236) for the non-anxious, mild, moderate, and severe anxiety groups, respectively (Table 5).

Table 5. Blood glucose preoperatively and postoperatively (mg/dL).

Anxiety category	Preoperative glucose (median, min–max)	Postoperative glucose (median, min–max)
Non-anxious	90 (78–136)	142 (118–248)
Mild anxiety	92.5 (66–111)	154.5 (125–238)
Moderate anxiety	90 (73–137)	178 (133–242)
Severe anxiety	110 (102–118)	223.5 (211–236)

Multivariable analysis

MANCOVA results are shown in Table 6. For NRS pain score outcomes, the coefficients (99% CI) and p-values were: 6 hours, 0.842 (0.475 to 1.209), $p < 0.001$; 12 hours, 0.381 (0.247 to 0.515), $p < 0.001$; and 24 hours, 0.158 (0.048 to 0.269), $p = 0.048$ (Table 6). For total opioid requirement at 24 hours, the coefficient was 147.8 (99% CI 124.062 to 171.651), $p < 0.001$ (Table 6). For postoperative NLR, the coefficient was 4.31 (99% CI 0.609 to 8.027), $p = 0.024$ (Table 6). For postoperative blood glucose, the coefficient was 19.4 (99% CI 7.912 to 30.912), $p = 0.001$ (Table 6).

Table 6. Association between preoperative anxiety and postoperative outcomes (MANCOVA).

Outcome	99% CI	Coefficient	P value
NRS pain score at 6 h	0.475 to 1.209	0.842	<0.001
NRS pain score at 12 h	0.247 to 0.515	0.381	<0.001
NRS pain score at 24 h	0.048 to 0.269	0.158	0.048
Total opioid requirement at 24 h	124.062 to 171.651	147.8	<0.001
Postoperative NLR	0.609 to 8.027	4.31	0.024
Postoperative blood glucose (mg/dL)	7.912 to 30.912	19.4	0.001

Discussion

Preoperative anxiety is frequent in surgical patients and, in the current study, higher anxiety was associated with higher postoperative pain and greater opioid requirement. This direction is consistent with published evidence.[11] A 2020 systematic review and meta-analysis reported a global pooled prevalence of preoperative anxiety of 48% across 28 studies (n = 14,652).[12] In a prospective cohort of laparoscopic gynecologic surgery (n = 330), 30% of patients met criteria for preoperative anxiety (APAIS > 10), and the anxiety group had higher postoperative pain within 48 hours and higher opioid (sufentanil) dose with more rescue analgesic use.[13] In elective surgical patients more broadly, one cohort study reported significantly higher postoperative pain in the high-anxiety group at 2, 4, 6, and 12 hours, with higher 24-hour tramadol consumption (156.5 ± 23.4 mg vs 147.1 ± 39 mg; p = 0.036).[14]

The clinical pattern observed in the current study fits core perioperative physiology. Anxiety increases sympathetic outflow and activates the hypothalamic-pituitary-adrenal axis, which raises catecholamines and cortisol.[15] This state can increase nociceptive gain, reduce descending inhibitory control, and promote central sensitization, so a given surgical stimulus is experienced as more painful and requires more opioid to achieve comparable comfort.[16] In gynecologic laparotomy, nociception comes from both somatic sources (abdominal wall incision and retraction, primarily via thoracoabdominal nerves) and visceral sources (uterine and adnexal manipulation, peritoneal irritation, and traction on pelvic structures).[17] When combined with stress-mediated hyperalgesia, these inputs can plausibly explain why anxious patients tend to report higher acute pain and need more analgesia, as reported in gynecologic and general surgical cohorts. Beyond the acute window, a 2025 systematic review and meta-analysis also found that preoperative anxiety was associated with chronic postsurgical pain, with a standardized mean difference of 0.31 (95% CI 0.20 to 0.41), supporting the concept that anxiety-related pain amplification can persist in some patients.[18]

The associations in the current study between anxiety and postoperative NLR and postoperative glucose are also clinically coherent with stress biology and anesthesia practice. NLR shifts are partly driven by cortisol and catecholamines, which increase circulating neutrophils while lowering lymphocytes, so higher perioperative stress can present as a higher NLR even without infection.[19] Postoperative hyperglycemia is similarly common after surgery because catecholamines and cortisol increase hepatic glucose production and insulin resistance, and pain itself can further intensify this response.[20] A recent review noted postoperative hyperglycemia occurs in about 40% of non-cardiac surgeries and 60% of cardiac surgeries.[21] Clinically, these literature benchmarks support integrating anxiety screening into routine preoperative assessment and linking it to interventions that target both pain pathways and stress response, such as structured education, appropriate anxiolysis when indicated, and opioid-sparing multimodal analgesia (for laparotomy, abdominal wall regional techniques plus non-opioid systemic agents), which are mechanistically suited to reduce sympathetic arousal, nociceptive amplification, and downstream metabolic and immune effects.

Study limitaitons

This study has several limitations. First, the single-center design with a relatively small sample limits generalizability, and the very small number of patients in the severe anxiety category the stability of estimates for that subgroup. Second, the observational nature of the analysis means causality cannot be established, and residual confounding is possible from factors that influence both anxiety and postoperative outcomes, such

as baseline pain sensitivity, prior chronic pain, depression or catastrophizing traits, sleep quality, and the complexity of the surgical pathology. Third, anxiety and pain are subjective measures and may be affected by reporting bias, while perioperative factors such as intraoperative anesthetic depth, postoperative analgesic administration patterns, and timing of laboratory measurements could introduce variability that is not fully captured in the available data.

Conclusion

Among women undergoing gynecologic laparotomy at Ngoerah Hospital, higher preoperative anxiety was associated with higher postoperative pain severity during the first 24 hours, greater postoperative opioid requirement, and higher postoperative neutrophil-to-lymphocyte ratio and blood glucose. These findings support incorporating preoperative anxiety screening into routine perioperative assessment and integrating anxiety-focused interventions, alongside opioid-sparing multimodal analgesia, as part of a clinically practical strategy to improve early postoperative outcomes in this population.

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