Journal of Medicine and Health (JMH)
Vol. 8 No. 2 August 2026
e-ISSN: 2442-5257
https://doi.org/10.28932/jmh.v8i2.14158

Research Article

Comparison of Combined Epidural-General Anesthesia and General Endotracheal Anesthesia on Neutrophil-Lymphocyte Ratio and Blood Sugar Levels in Colorectal Surgery

Perbandingan *Combined Epidural-General Anesthesia dan General Endotracheal Anesthesia* terhadap Rasio Neutrofil-Limfosit dan Kadar Gula Darah pada Operasi Kolorektal

Wawan Susilo[1]*, Faisal Sommeng[1], Imam Hermansyah[2]
[1]Department of Anesthesiology, Faculty of Medicine, Universitas Muslim Indonesia, Rumah Sakit Umum Ibnu Sina, YW-UMI, Sulawesi Selatan, Indonesia
Jl. Urip Sumoharjo, KM. 5. Makassar, Sulawesi Selatan 90231
[2]Rumah Sakit Umum Daerah Sinjai, Sulawesi Selatan, Indonesia
Jl. Jenderal Sudirman No. 47 Sinjai Sulawesi Selatan, 92615
**Correspondence author*
Email: wawan.susilo@umi.ac.id

Received: December 21, 2025
Accepted: June 30, 2026

Abstract

Colorectal surgery induces systemic inflammatory and neuroendocrine stress responses that may affect postoperative outcomes. The neutrophil–lymphocyte ratio (NLR) and random blood glucose (RBG) levels are simple biomarkers for assessing perioperative inflammatory and metabolic stress. Combined epidural–general anesthesia (CEGA) is presumed to better attenuate these responses than general endotracheal anesthesia (GETA). This randomized controlled trial compared the effects of CEGA and GETA on perioperative changes in NLR and RBG in patients undergoing colorectal surgery. A total of 24 patients with American Society of Anesthesiologists (ASA) physical status I–II were randomly assigned to the CEGA (n = 12) or GETA (n = 12) group. NLR and RBG were measured preoperatively and at 6 and 24 hours postoperatively. Both groups demonstrated significant increases in NLR and RBG at 6 hours after surgery, followed by a decline at 24 hours. However, NLR at 24 hours postoperatively was significantly lower in the CEGA group than in the GETA group (p = 0.009). RBG levels were also significantly lower in the CEGA group at 6 hours (p = 0.012) and 24 hours postoperatively (p = 0.007). These findings indicate that CEGA is more effective than GETA in attenuating inflammatory and metabolic stress responses in colorectal surgery.

Keywords*: blood glucose; colorectal surgery; combined epidural–general anesthesia; general endotracheal anesthesia; neutrophil–lymphocyte ratio.*

How to Cite:
Susilo W, Sommeng F, Hermansyah I. Comparison of combined epidural–general anesthesia and general endotracheal anesthesia on neutrophil–lymphocyte ratio and blood sugar levels in colorectal surgery. Journal of Medicine and Health. 2026; 8(2): 139-46. DOI: https://doi.org/10.28932/jmh.v8i2.14158.

Research Article

Introduction

Colorectal surgery is a major surgical procedure associated with substantial tissue injury, resulting in systemic inflammatory and neuroendocrine stress responses that influence postoperative outcomes.[1] Surgical trauma triggers an early release of pro-inflammatory cytokines within hours after incision, triggering activation of innate immune pathways. Concurrently, nociceptive stimulation and operative stress activate the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system, leading to increased cortisol secretion and metabolic disturbances, particularly stress-induced hyperglycemia.[2,3] These interconnected inflammatory and endocrine mechanisms represent key determinants of perioperative physiological adaptation and recovery following colorectal procedures.

Among the biomarkers used to evaluate perioperative physiological stress, the neutrophil–lymphocyte ratio (NLR) and random blood glucose (RBG) are widely recognized due to their accessibility, low cost, and clinical applicability in routine perioperative practice. NLR serves as a practical surrogate marker of systemic inflammation and has shown good correlation with established inflammatory biomarkers such as C-reactive protein (CRP) and interleukin-6 (IL-6), while RBG reflects the neuroendocrine stress response associated with inflammatory activation.[4,5] Elevated NLR reflects an imbalance toward innate inflammatory activity with suppression of adaptive immunity, whereas increased RBG indicates stress hormone–mediated metabolic dysregulation, driven mainly by cortisol and catecholamines through increased gluconeogenesis and insulin resistance. Excessive inflammatory and metabolic stress responses are associated with immune impairment, increased postoperative complications, delayed wound healing, and prolonged hospitalization in patients undergoing colorectal surgery.[4–6]

Beyond their role as indicators of surgical stress, both NLR and hyperglycemia have been implicated in colorectal cancer progression and postoperative recovery. Increased NLR, measured either locally within the tumor microenvironment or systemically through peripheral blood, has been associated with reduced survival and poorer prognosis in colorectal cancer patients. This observation suggests that neutrophil-dominant inflammatory responses accompanied by reduced lymphocyte-mediated immunity contribute to tumor progression, increased biological aggressiveness, and potential resistance to therapy.[7,8] Likewise, hyperglycemia may not only facilitate colorectal cancer progression but also impair anastomotic healing through mechanisms involving oxidative stress, inflammatory dysregulation, and disrupted tissue regeneration. Activation of the PI3K/AKT/mTOR signaling pathway and alterations in the tissue

Research Article

microenvironment under hyperglycemic conditions may reduce collagen deposition, angiogenesis, and tissue integrity, thereby increasing the risk of anastomotic leakage.[9,10]

Anesthetic technique plays a pivotal role in modulating perioperative stress responses. General endotracheal anesthesia (GETA) without neuraxial blockade permits greater sympathetic activation and stress hormone release. In contrast, combined epidural–general anesthesia (CEGA) provides effective sympathetic blockade and attenuates nociceptive transmission from the surgical field, thereby reducing pro-inflammatory cytokine release and neuroendocrine stress responses.[11–13] Therefore, this study aims to compare the physiological effects of CEGA and GETA on perioperative inflammatory and metabolic responses in patients undergoing colorectal surgery.

Methods

This study was conducted as a randomized controlled trial after obtaining ethical approval from the Biomedical Research Ethics Committee of the Faculty of Medicine, Hasanuddin University (No: 533/UN4.6.5.4.31/PP36/2024). The study was carried out at Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia.

Inclusion criteria comprised adult patients undergoing colorectal surgery (colorectal cancer) with American Society of Anesthesiologists (ASA) physical status I–II and a body mass index (BMI) between 18 and 34 kg/m². Exclusion criteria included contraindications to epidural anesthesia, immunological disorders, adrenal hormone dysfunction, chronic use of anti-inflammatory medications, hypovolemic shock, delayed extubation, and death during the postoperative period.

Eligible patients were randomly allocated into two groups: General Endotracheal Anesthesia (GETA) or Combined Epidural–General Anesthesia (CEGA). Randomization was performed using a simple lottery method to ensure equal allocation.

Patients in the CEGA group received premedication with fentanyl 2–3 µg/kg intravenously (IV), followed by induction using propofol 1–2.5 mg/kg body weight (BW) IV. Endotracheal intubation was facilitated with atracurium 0.5 mg/kg BW IV and 1% lidocaine 1 mg/kg BW IV. Epidural anesthesia was then performed, targeting a sensory block from T6 to S2 (14 dermatomes). The epidural catheter was planned for insertion at the T9–T10 intervertebral space, with an estimated local anesthetic volume of 1.2 mL per dermatome, resulting in a total volume of 16.8 mL. The epidural solution consisted of 0.25% isobaric bupivacaine (42 mg) combined with fentanyl 50 µg, with the total bupivacaine dose remaining below the maximum recommended toxic dose of 195 mg. Patients in the GETA group received premedication with

Research Article

fentanyl 2–3 µg/kg IV, followed by induction using propofol 1–2.5 mg/kg BW IV. Endotracheal intubation was facilitated with atracurium 0.5 mg/kg BW IV and 1% lidocaine 1 mg/kg BW IV.

Blood samples were collected prior to intervention (baseline) and at 6 and 24 hours postoperatively to measure random blood glucose (RBG) levels and the neutrophil–lymphocyte ratio (NLR). Data are presented as mean ± standard deviation (SD). Statistical analysis was performed using repeated-measures ANOVA and the independent t-test for normally distributed data, while the Friedman test and Mann–Whitney U test were applied for non-normally distributed variables. A p-value < 0.05 was considered statistically significant.

Results

Patient characteristics in this study are presented in Table 1. Perioperative changes in Neutrophil–Lymphocyte Ratio (NLR) and random blood glucose are shown in Table 2.

Table 1 Patient Characteristics

Variable	GETA (n=12)	CEGA (n=12)	p-value
Sex			
Female	8 (66.7%)	8 (66.7%)	1.000[a]
Male	4 (33.3%)	4 (33.3%)	
Age (years)	50.25 ± 19.44	55.17 ± 11.01	0.931[b]
Body mass index (kg/m^2)	20.93 ± 3.03	21.77 ± 1.78	0.416[c]
Duration of anesthesia (min)	207.50 ± 21.37	202.50 ± 16.58	0.529[c]
Hypertension	3 (25.0%)	4 (33.3%)	0.653[a]
Type 2 Diabetes	4 (33.3%)	2 (16.7%)	0.346[a]

(a) Chi-square test; (b) Mann-Whitney test; (c) Independent t-test

Table 2 Perioperative Changes in Neutrophil–Lymphocyte Ratio (NLR) and Random Blood Glucose

Variable	CEGA (n=12) (Mean ± SD)	GETA (n=12) (Mean ± SD)	*p-value*
Neutrophil–Lymphocyte Ratio			
Preoperative (baseline)	2.89 ± 1.42	2.74 ± 1.45	0.817[a]
6 hours postoperatively	11.83 ± 6.80	14.90 ± 10.26	0.525[a]
24 hours postoperatively	6.38 ± 3.04	9.73 ± 2.66	0.009[b*]
p-value	0.001[c*]	<0.001[d*]	
Random Blood Glucose Levels (mg/dL)			
Preoperative (baseline)	118.50 ± 30.93	119.25 ± 22.53	0.946[b]
6 hours postoperatively	128.67 ± 30.67	171.75 ± 50.24	0.012[a*]
24 hours postoperatively	106.83 ± 16.06	155.92 ± 54.41	0.007[a*]
p-value	0.001[c*]	0.017[d*]	

(a) Mann-Whitney test; (b) Independent t-test; (c) Repeated-measures ANOVA test; (d) Friedman test

Research Article

In the CEGA group, significant changes over time were observed in both NLR (p = 0.001) and RBG levels (p = 0.001). Mean NLR increased to 11.83 ± 6.80 at 6 hours postoperatively and subsequently decreased to 6.38 ± 3.04 at 24 hours. Similarly, mean RBG levels increased to 128.67 ± 30.67 mg/dL at 6 hours and declined to 106.83 ± 16.06 mg/dL at 24 hours postoperatively.

Comparable temporal changes were observed in the GETA group, with significant differences in NLR (p < 0.001) and RBG levels (p = 0.017). Mean NLR increased to 14.90 ± 10.26 at 6 hours postoperatively and decreased to 9.73 ± 2.66 at 24 hours. Mean RBG levels rose to 171.75 ± 50.24 mg/dL at 6 hours and declined to 155.92 ± 54.41 mg/dL at 24 hours postoperatively.

Between-group comparisons demonstrated significantly lower NLR values in the CEGA group at 24 hours postoperatively compared with the GETA group (6.38 ± 3.04 vs 9.73 ± 2.66; p = 0.009). RBG levels were also significantly lower in the CEGA group at both 6 hours (128.67 ± 30.67 mg/dL vs 171.75 ± 50.24 mg/dL; p = 0.012) and 24 hours postoperatively (106.83 ± 16.06 mg/dL vs 155.92 ± 54.41 mg/dL; p = 0.007).

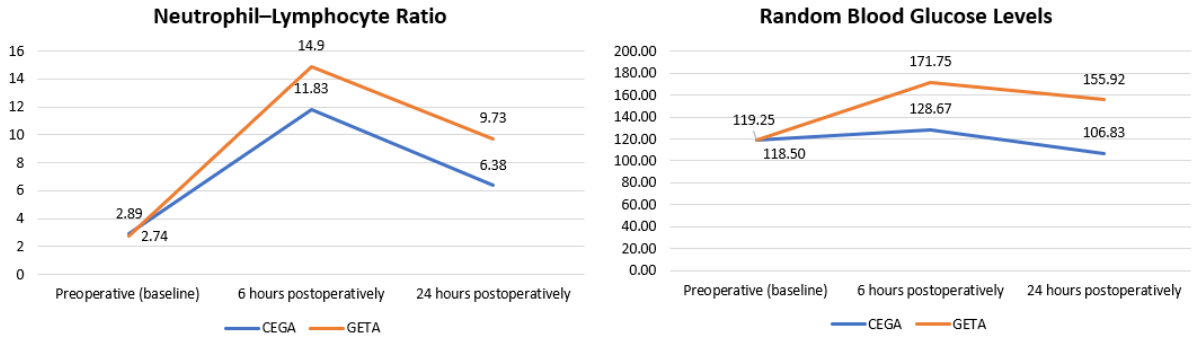

Figure 1 Perioperative Changes in NLR and Random Blood Glucose Levels

Discussion

Significant changes in NLR values were observed in both groups. NLR increased at 6 hours postoperatively and subsequently decreased at 24 hours postoperatively. Between-group analysis demonstrated that NLR values were significantly higher in the GETA group compared with the CEGA group at 24 hours postoperatively. Similar findings have been reported in previous studies. Hazar and Altinisik (2024) observed a significant increase in NLR values during the perioperative period in both groups, with median NLR significantly higher in the CS-GA group.[14]

The increase in NLR at 6 hours postoperatively in both groups reflects an acute inflammatory response to surgical trauma. The subsequent decline in NLR at 24 hours

postoperatively suggests early resolution of inflammation. However, the persistently higher NLR values observed in the GETA group compared with the CEGA group indicate a more sustained inflammatory response in patients receiving general anesthesia without neuraxial blockade, as well as a more rapid recovery of immune function in the CEGA group.

No significant difference in baseline RBG levels was observed between the CEGA and GETA groups, indicating comparable baseline metabolic conditions. At 6 hours postoperatively, RBG levels increased significantly in both groups, with significantly higher values observed in the GETA group compared with the CEGA group. This difference persisted at 24 hours postoperatively, where RBG levels in the GETA group remained significantly higher than those in the CEGA group.

Consistent with these findings, previous studies have reported a progressive increase in blood glucose levels in both groups during the postoperative period. However, the magnitude of hyperglycemia was greater in the GETA group, becoming evident early after surgery and persisting up to 24 hours postoperatively.[5] These findings suggest that postoperative hyperglycemic responses are more pronounced and sustained in patients undergoing general endotracheal anesthesia without neuraxial blockade.

Combined epidural–general anesthesia provides perioperative benefits through several mechanisms. This anesthetic technique is more effective in alleviating acute pain and mitigating pain-related adverse effects, while attenuating excessive neuroendocrine, metabolic, and inflammatory responses following surgery. The use of local anesthetics has been shown to inhibit neutrophil and macrophage activation, thereby suppressing exaggerated inflammatory responses.[5,15]

During surgery, activation of the hypothalamic–pituitary–adrenal axis and the sympathetic nervous system occurs through hypovolemia-induced baroreceptor stimulation, afferent nociceptive impulses from the surgical site, and cytokine release induced by tissue trauma. Postoperative psychological stress further increases cortisol secretion, contributing to elevated blood glucose levels. Activation of the HPA axis via stimulation of the paraventricular nucleus triggers adrenocorticotropic hormone (ACTH) release and enhances adrenal cortisol production, which has been reported to peak within 4–6 hours postoperatively and may remain elevated for several days following major surgery.[16–18]

The lower postoperative blood glucose levels observed in the CEGA group indicate that this anesthetic technique effectively attenuates surgical stress responses by suppressing afferent nerve impulses and autonomic nervous system activation associated with pain, which are key triggers of neuroendocrine stress responses.[5]

Research Article

Furthermore, the combination of epidural and general anesthesia has been reported to provide superior hemodynamic stability and reduced opioid requirements compared with general anesthesia alone. In patients undergoing colorectal surgery, thoracic epidural anesthesia has also been shown to promote early mobilization and faster recovery of bowel function, thereby reducing gastrointestinal complications.[19,20]

Several limitations of this study should be acknowledged. These include the absence of evaluation of surgical duration, types of colorectal procedures, and intraoperative hemodynamic changes. Additionally, the relatively small sample size compared with other studies may limit the generalizability of the findings.

Conclusion

Combined epidural–general anesthesia (CEGA) is superior to general endotracheal anesthesia (GETA) in attenuating inflammatory responses and metabolic stress responses in patients undergoing colorectal surgery.

References

1. Mari G, Costanzi A, Crippa J, Falbo R., Miranda A., Rossi M, et al. Surgical stress reduction in elderly patients undergoing elective colorectal laparoscopic surgery within an ERAS protocol. Chirurgia (Romania). 2016;111(6):476-480. doi:10.21614/chirurgia.111.6.476
2. Tohme S, Simmons RL, Tsung A. Surgery for cancer: A trigger for metastases. Cancer Res. 2017;77(7):1548-1552. doi:10.1158/0008-5472.CAN-16-1536
3. Cusack B, Buggy DJ. Anaesthesia, analgesia, and the surgical stress response. BJA Educ. 2020;20(9). doi:10.1016/j.bjae.2020.04.006
4. Aykut A. Potential Role of Erector Spinae Plane Block on Neutrophil-Lymphocyte Ratio in Cardiac Surgery Patients. J Cardiovasc-Thorac Anaesth Intensive Care Soc. 2023;29(3):141-147. doi:10.14744/gkdad.2023.75010
5. Sağlık Y, Yazıcıoğlu D, Çiçekler O, Gümüş H. Investigation of Effects of Epidural Anaesthesia Combined with General Anaesthesia on the Stress Response in Patients Undergoing Hip and Knee Arthroplasty. Turk Anesteziyoloji ve Reanimasyon Dernegi Dergisi. 2015;43(3):154-161. doi:10.5152/TJAR.2015.26818
6. Hou BJ, Du Y, Gu SX, Fan J, Wang R, Deng H, Guo DX, et al. General anesthesia combined with epidural anesthesia maintaining appropriate anesthesia depth may protect excessive production of inflammatory cytokines and stress hormones in colon cancer patients during and after surgery. *Medicine*. 2019;98(30):1-5. doi:10.1097/MD.0000000000016610
7. Gonzales Stuva JP, Pérez-López C, Ramírez Romero MS, et al. Hematological markers as prognostic predictors in patients undergoing colon cancer surgery. Sci Rep. 2025;15(1). doi:10.1038/s41598-025-33554-x
8. Xun F, Jiang W, Sha M, Wang W, Xia Y, Hu H, Liu R, et al. Neutrophil-to-lymphocyte ratio in colorectal tissue affects prognosis in patients with colorectal cancer. Pathology. 2024;56(5):643-652. doi:10.1016/j.pathol.2024.03.003
9. Cai XJ, Zhang JY, Zhang AB, Zhou X, Zhang HY, Li TJ. Emerging Role of High Glucose Levels in Cancer Progression and Therapy. Chin J Dent Res. 2022;25(1):11-20. doi:10.3290/j.cjdr.b2752695
10. Li F, Wan X, Li Z, Zhou L. High glucose inhibits autophagy and promotes the proliferation and metastasis of colorectal cancer through the PI3K/AKT/mTOR pathway. Cancer Med. 2024;13(11). doi:10.1002/cam4.7382
11. Shen Y, Chen X, Hou J, Chen Y, Fang Y, Xue Z, D'Journo XB, et al. The effect of enhanced recovery after minimally invasive esophagectomy: a randomized controlled trial. Surg Endosc. 2022;36(12):9113-9122. doi:10.1007/s00464-022-09385-6
12. Lin EJ, Prost S, Lin HJ, Shah S, Li R. Combined General/Epidural Anesthesia vs. General Anesthesia on Postoperative Cytokines: A Review and Meta-Analysis. Cancers (Basel). 2025;17(10):1667. doi:10.3390/cancers17101667

Research Article

13. Reysner T, Wieczorowska-Tobis K, Kowalski G, Grochowicka M, Pyszczorska M, Mularski A, Reysner M. The Influence of Regional Anesthesia on the Systemic Stress Response. Reports. 2024;7(4):89. doi:10.3390/reports7040089
14. Hazar EÜ, Altınışık HB. Comparison of the effects of normal and cesarean delivery methods and general and spinal anesthesia techniques on the inflammatory response. Anaesth Pain Intensi. 2024;28(6):1017. doi:10.35975/apic.v28i6.2608
15. Li N, Kong H, Li SL, Zhu SN, Wang DX. Combined epidural-general anesthesia was associated with lower risk of postoperative complications in patients undergoing open abdominal surgery for pheochromocytoma: A retrospective cohort study. PLoS One. 2018;13(2):1-13. doi:10.1371/journal.pone.0192924
16. Prete A, Yan Q, Al-Tarrah K, Akturk HK, Prokop LJ, Alahdab F, Foster MA, et al. The cortisol stress response induced by surgery: A systematic review and meta-analysis. Clin Endocrinol (Oxf). Blackwell Publishing Ltd. 2018;89(5):554-567. doi:10.1111/cen.13820
17. Ivascu R, Torsin LI, Hostiuc L, Nitipir C, Corneci D, Dutu M. The Surgical Stress Response and Anesthesia: A Narrative Review. J Clin Med. Blackwell Publishing Ltd. 2024;13(10). doi:10.3390/jcm13103017
18. Kelliher LJS, Scott M. Modifying the Stress Response – Perioperative Considerations and Controversies. Anesthesiol Clin. 2022;40(1). doi:10.1016/j.anclin.2021.11.012
19. Elsayed AA, El-deen NMG, Shams GHR, Aly AEA, Mohammed WS. Comparative Study between General Anesthesia versus General Anesthesia Combined with Thoracic Epidural Analgesia on Cytokine Response in Laparoscopic Cholecystectomy Patients. Open J Anesthesiol. 2020;10(06):247-262. doi:10.4236/ojanes.2020.106022
20. Pei JP, Zhang CD, Liang Y, Zhang C, Wu KZ, et al. Effects of epidural combined with general anesthesia versus general anesthesia alone in gastric cancer surgery: a propensity score matching analysis. Ann Transl Med. 2020;8(7):473-473. doi:10.21037/atm.2020.03.127