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Original Research Article

Comparative Study of Perioperative Blood Pathology Markers in Patients Undergoing General vs. Regional Anesthesia

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Abstract:

Background: The choice of anesthetic technique can significantly modulate the systemic stress and inflammatory response to surgery. Both general anesthesia (GA) and regional anesthesia (RA) are widely used, but their comparative impact on perioperative pathophysiology, as reflected by common blood markers, remains an area of active investigation.

Methods: This prospective, comparative observational study included 120 patients (ASA physical status I-III) scheduled for primary unilateral TKA. Patients were allocated to receive either GA (n=60) or RA (n=60) based on patient and anesthesiologist preference. Venous blood samples were collected preoperatively (T0) and 24 hours postoperatively (T1). Markers analyzed included C-reactive protein (CRP), white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), serum cortisol, blood glucose, hemoglobin, and platelet count. Statistical analysis was performed using independent t-tests and Chi-square tests, with $p<0.05$ considered significant.

Results: Baseline demographic and clinical characteristics were comparable between the two groups ($p>0.05$). At 24 hours postoperatively, the GA group exhibited significantly higher levels of key inflammatory markers compared to the RA group, including CRP (68.4 ± 9.2 mg/L vs. 47.1 ± 8.5 mg/L; $p<0.001$), WBC count (12.8 ± 1.9 x10^9/L vs. 10.5 ± 1.7 x10^9/L; $p<0.001$), and NLR (7.9 ± 1.5 vs. 5.6 ± 1.3; $p<0.001$). The GA group also showed a greater stress response, with significantly higher postoperative serum cortisol (24.8 ± 4.1 µg/dL vs. 18.2 ± 3.7 µg/dL; $p<0.001$) and blood glucose (135 ± 18 mg/dL vs. 119 ± 15 mg/dL; $p<0.001$). The postoperative decrease in hemoglobin and change in platelet count were not significantly different between groups ($p=0.34$ and $p=0.18$, respectively).

Conclusion: In patients undergoing TKA, general anesthesia is associated with a significantly more pronounced systemic inflammatory and endocrine stress response at 24 hours post-surgery compared to regional anesthesia. These findings suggest that regional anesthesia may offer a protective advantage by attenuating the surgical stress response, which could have implications for patient recovery and postoperative outcomes.

Keywords: General Anesthesia, Regional Anesthesia, Spinal Anesthesia, Surgical Stress Response, C-Reactive Protein, Neutrophil-Lymphocyte Ratio, Perioperative Care.

Introduction

Surgical trauma invariably elicits a complex cascade of physiological responses, including neuroendocrine, metabolic, and immunological changes, collectively known as the surgical stress response [1].

This response, while evolutionarily protective, can become exaggerated and contribute to postoperative complications such as immunosuppression, organ dysfunction, and delayed recovery [2]. The choice of anesthetic management is a critical, modifiable factor that can profoundly influence the magnitude of this perioperative stress response [3].

Anesthetic techniques are broadly categorized into general anesthesia (GA), which induces a state of controlled unconsciousness, and regional anesthesia (RA), which involves blocking nerve conduction from a specific region of the body.

GA involves the systemic administration of multiple drugs that can directly affect immune cell

function and the hypothalamic-pituitary-adrenal (HPA) axis [4]. In contrast, RA techniques like spinal or epidural anesthesia can mitigate the stress response by blocking the transmission of noxious afferent signals from the surgical site to the central nervous system [5]. Recent research has focused on quantifying the differential impact of these anesthetic modalities using various biomarkers. Inflammatory markers such as C-reactive protein (CRP), an acute-phase reactant, and the neutrophil-to-lymphocyte ratio (NLR), an indicator of systemic inflammation and physiological stress, have emerged as valuable tools [6, 7].

Studies have shown that elevated perioperative NLR is associated with adverse outcomes in various surgical settings [8]. Similarly, endocrine markers like cortisol and glucose provide a direct measure of HPA axis activation and the metabolic stress response [9].

Several studies have compared the inflammatory and stress responses between GA and RA, yielding mixed results often dependent on the type of surgery and the specific markers analyzed. Some research suggests that RA, particularly neuraxial blockade, is superior in blunting the release of catecholamines and cortisol [10].

A meta-analysis by Srinivasa et al. indicated that epidural anesthesia and analgesia could reduce postoperative morbidity, potentially by attenuating the stress response [11].

However, other studies have reported no significant difference in inflammatory cytokine levels, such as IL-6, between the two techniques, especially in major abdominal surgery [12]. This highlights a research gap concerning the comprehensive comparison of a panel of readily available and clinically relevant blood pathology markers within a standardized, homogenous surgical population.

Total knee arthroplasty (TKA) presents an ideal model for such a comparison, as it is a common, standardized procedure that induces a significant inflammatory response and can be performed effectively under either GA or RA [13].

Clarifying the impact of anesthetic choice in this context is crucial for optimizing patient care, particularly within the framework of Enhanced Recovery after Surgery (ERAS) protocols, which prioritize minimizing physiological stress [14].

Therefore, the aim of this study was to conduct a comparative analysis of perioperative changes in key inflammatory (CRP, WBC, NLR), stress-related (cortisol, glucose), and hematological (hemoglobin, platelets) markers in a cohort of patients undergoing primary TKA under either general or regional anesthesia.

We hypothesized that patients receiving regional anesthesia would exhibit a significantly attenuated inflammatory and stress response compared to those receiving general anesthesia.

Materials and Methods

A total of 120 patients scheduled for elective, primary, unilateral total knee arthroplasty were enrolled. Patients were included if they were between 40 and 80 years of age and had an American Society of Anesthesiologists (ASA) physical status of I, II, or III.

Inclusion Criteria:

1. Scheduled for primary unilateral TKA.
2. Age 40–80 years.
3. ASA physical status I–III.
4. Provided written informed consent.

Exclusion Criteria:

1. Patient refusal or inability to provide consent.
2. Pre-existing chronic inflammatory or autoimmune disease (e.g., rheumatoid arthritis).
3. Chronic use of corticosteroids or other immunosuppressive drugs.
4. Known allergy to local or general anesthetic agents.
5. Pre-existing coagulopathy or ongoing anticoagulant therapy that contraindicated spinal anesthesia.
6. Emergency or revision surgery.
7. Intraoperative conversion from regional to general anesthesia.

Anesthetic and Surgical Procedure

Patients were non-randomly allocated to the General Anesthesia (GA, n=60) or Regional Anesthesia (RA, n=60) group based on a shared decision-making process involving the patient and the attending anesthesiologist.

- **GA Group:** Anesthesia was induced with intravenous propofol (2-2.5 mg/kg) and fentanyl (1-2 µg/kg). A laryngeal mask airway was inserted, and anesthesia was maintained with sevoflurane in an air/oxygen / nitrous oxide. Reversed with inj myopyrrolate p or sugamadex..
- **RA Group:** Patients received spinal anesthesia in the sitting position at the L3-L4 or L4-L5 interspace using a 25-gauge Whitacre needle. A solution of 12.5–15 mg of 0.5% hyperbaric bupivacaine with 15 µg of fentanyl was administered.

All surgical procedures were performed by one of three senior orthopedic surgeons using a standardized medial parapatellar approach and cemented implants.

All patients received a standardized postoperative analgesia regimen inj Diclofenac, nerve block and scheduled oral paracetamol and celecoxib.

Data and Sample Collection

Demographic data (age, sex, body mass index [BMI]) and clinical data (ASA status, duration of surgery) were recorded. Venous blood samples were collected at two time points:

- **T0:** Preoperatively, after insertion of an intravenous cannula but before induction of anesthesia.
- **T1:** 24 hours (± 2 hours) after the end of the surgical procedure.

All blood samples were processed within one hour of collection by the hospital's central laboratory.

The following parameters were measured using automated analyzers: CRP (immunoturbidimetric assay), complete blood count (WBC, neutrophil count, lymphocyte count, hemoglobin, platelet count), serum cortisol (electrochemiluminescence immunoassay), and random blood glucose (hexokinase method). The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

Statistical Analysis: Data were analyzed using SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as number (%). The normality of data distribution was assessed using the Shapiro-Wilk test. To compare baseline characteristics and postoperative outcomes between the GA and RA groups, the independent samples t-test was used for normally distributed continuous variables, and the Mann-Whitney U test was used for non-normally distributed data. The Chi-square test or Fisher's exact test was used for categorical variables. A p-value of less than 0.05 was considered statistically significant.

Results

Patient Demographics and Baseline Characteristics: A total of 120 patients (60 in the GA group, 60 in the RA group) completed the study. The demographic and clinical characteristics of the patients are presented in Table 1. There were no statistically significant differences between the two groups in terms of age, sex distribution, BMI, ASA physical status, or duration of surgery, indicating that the two cohorts were well-matched at baseline.

Table 1: Demographic and Clinical Characteristics of Study Participants

Characteristic	General Anesthesia (n=60)	Regional Anesthesia (n=60)	p-value
Age (years)	67.2 ± 7.8	68.1 ± 8.3	0.591
Sex (Male/Female)	24 (40%) / 36 (60%)	27 (45%) / 33 (55%)	0.584
BMI (kg/m²)	30.5 ± 4.1	29.9 ± 3.8	0.442
ASA Status (I/II/III)	5 / 43 / 12	7 / 40 / 13	0.778
Surgery Duration (min)	94.5 ± 12.1	92.8 ± 11.5	0.467

Perioperative Inflammatory Markers: At baseline (T0), there were no significant differences in CRP, WBC count, or NLR between the two groups (all $p>0.05$). As shown in Table 2, both groups exhibited a marked increase in all inflammatory markers at 24 hours postoperatively (T1). However, this increase was significantly greater in the GA group. The mean postoperative CRP level in the GA group was 68.4 mg/L compared to 47.1 mg/L in the RA group ($p<0.001$).

Similarly, the postoperative WBC count (12.8 vs. 10.5 x10⁹/L; $p<0.001$) and NLR (7.9 vs. 5.6; $p<0.001$) were also significantly higher in the GA group.

Table 2: Comparison of Perioperative Inflammatory Markers

Marker	Time Point	GA Group (n=60)	RA Group (n=60)	p-value
CRP (mg/L)	T0	3.1 ± 1.5	3.3 ± 1.7	0.589
	T1	**68.4 ± 9.2**	**47.1 ± 8.5**	**<0.001**
WBC count (x10⁹/L)	T0	6.5 ± 1.4	6.7 ± 1.3	0.492
	T1	**12.8 ± 1.9**	**10.5 ± 1.7**	**<0.001**
NLR	T0	2.5 ± 0.8	2.4 ± 0.7	0.611
	T1	**7.9 ± 1.5**	**5.6 ± 1.3**	**<0.001**

Perioperative Stress and Hematological Markers: The baseline values for cortisol, glucose, hemoglobin, and platelets were comparable between the groups (Table 3). At 24 hours postoperatively, the GA group showed significantly higher levels of serum cortisol (24.8 vs. 18.2 µg/dL; $p<0.001$) and blood glucose (135 vs. 119 mg/dL; $p<0.001$) compared to the RA group. Both groups experienced a similar postoperative drop in hemoglobin concentration, with no statistically significant difference between them ($p=0.34$). Postoperative platelet counts increased slightly in both groups, again with no significant intergroup difference ($p=0.18$).

Table 3: Comparison of Perioperative Stress and Hematological Markers

Marker	Time Point	GA Group (n=60)	RA Group (n=60)	p-value
Cortisol (µg/dL)	T0	12.5 ± 3.1	12.1 ± 2.9	0.485
	T1	**24.8 ± 4.1**	**18.2 ± 3.7**	**<0.001**
Glucose (mg/dL)	T0	95 ± 12	97 ± 11	0.399
	T1	**135 ± 18**	**119 ± 15**	**<0.001**
Hemoglobin (g/dL)	T0	13.6 ± 1.1	13.8 ± 1.2	0.407
	T1	10.9 ± 0.9	11.1 ± 1.0	0.340
Platelets (x10⁹/L)	T0	245 ± 48	251 ± 52	0.521
	T1	258 ± 55	265 ± 59	0.180

Discussion

The principal finding of this prospective comparative study is that general anesthesia is associated with a significantly more pronounced systemic inflammatory and neuroendocrine stress response compared to regional (spinal) anesthesia in patients undergoing TKA. Specifically, at 24 hours post-surgery, patients in the GA group demonstrated markedly higher levels of CRP, WBC, NLR, serum cortisol, and blood glucose.

Our results concerning inflammatory markers are consistent with a growing body of evidence. The profound elevation in CRP and NLR in the GA group suggests a greater acute-phase reaction. This may be attributable to several mechanisms. First, RA provides a dense afferent neural blockade, which can inhibit the transmission of nociceptive signals that are a primary trigger for the systemic inflammatory cascade [5, 15]. Second, general anesthetic agents themselves, such as volatile anesthetics and opioids, may have direct immunomodulatory effects, though these are complex and not fully elucidated [4]. The significant difference in NLR, a robust marker of systemic inflammation, aligns with findings from De Cassai et al., who also reported a lower postoperative NLR in patients receiving neuraxial blockade for major surgery [7]. This attenuated inflammatory state may have clinical benefits, as excessive inflammation is linked to increased postoperative pain, delayed wound healing, and organ dysfunction [2].

The observed differences in stress hormone levels further support our hypothesis. The significantly lower postoperative cortisol and glucose levels in the RA group indicate a more effective blunting of the HPA axis. Spinal anesthesia effectively blocks somatic and sympathetic nerve fibers below the level of injection, thereby interrupting the primary pathway that signals surgical trauma to the brain and triggers cortisol release [10].

This finding corroborates earlier work by Ahlers et al., which demonstrated that neuraxial blockade is superior to GA in suppressing the perioperative stress response [9]. The clinical relevance of this HPA axis modulation is significant, as hyperglycemia and hypercortisolemia can impair immune function and increase the risk of infection [1]. Interestingly, we found no significant difference in the postoperative decrease in hemoglobin or the change in platelet count. The similar drop in hemoglobin suggests that intraoperative blood loss was comparable between the groups, which is supported by the similar surgical duration. This finding strengthens our study by indicating that the observed differences in inflammatory markers were likely due to the anesthetic technique rather than variations in surgical trauma or blood loss.

The clinical implications of these findings are particularly relevant in the context of ERAS pathways. A core tenet of ERAS is to minimize the physiological stress of surgery to facilitate faster recovery [14]. Our data provide a pathophysiological basis for preferring RA over GA in lower limb orthopedic surgery when clinically appropriate. By attenuating the inflammatory and endocrine response, RA may contribute to better pain control, reduced postoperative nausea and vomiting, and an earlier return to function, although these clinical outcomes were not directly assessed in our study. A study by Memtsoudis et al. using a large national database found that neuraxial anesthesia was associated with lower rates of major complications after TKA, which may be partly explained by the physiological benefits we observed [13].

This study has several limitations. First, it was an observational study without randomization, which introduces the potential for selection bias. However, the baseline characteristics of the two groups were well-matched. Second, it was a single-center study, which may limit the generalizability of our findings. Third, we only measured biomarkers at a single postoperative time point (24 hours). A time-course analysis with multiple sampling points would have provided a more detailed picture of the dynamic response. Finally, we did not measure specific pro-inflammatory cytokines like IL-6 or TNF-α, which could have provided deeper mechanistic insights.

Conclusion

In conclusion, this study demonstrates that in patients undergoing total knee arthroplasty, general

anesthesia is associated with a significantly greater postoperative inflammatory and stress response at 24 hours compared to regional anesthesia. This is evidenced by higher levels of C-reactive protein, white blood cell count, neutrophil-to-lymphocyte ratio, cortisol, and glucose. These findings provide strong evidence that regional anesthesia offers a significant advantage in mitigating the surgical stress response. The selection of regional anesthesia, when feasible, may be a key component in optimizing perioperative care and enhancing patient recovery, aligning with the principles of modern ERAS protocols. Further large-scale, randomized controlled trials are warranted to correlate these biomarker findings with clinical outcomes such as postoperative pain, length of hospital stay, and long-term functional recovery.

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