RESEARCH PAPER

Perioperative Angiogenic and Inflammatory Biomarker Responses to Sevoflurane and Propofol in Lung Cancer Patients Undergoing Diagnostic Bronchoscopy

Johannas[1,2], Efrida[3], Masrul Basyar[4], Eryati Darwin[5]

[1]Doctoral Program of Biomedical Science, Faculty of Medicine, University of Andalas, Padang 25171, Indonesia
[2]Department of Anesthesiology and Intensive Care, Faculty of Medicine, University of Riau, 28133, Indonesia
[3]Department of Clinical Pathology and Laboratory Medicine, Faculty of Medicine, Universitas Andalas / M. Djamil General Hospital, Padang, 25171, West Sumatera, Indonesia
[4]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Andalas / M. Djamil General Hospital, Padang, 25171, West Sumatera, Indonesia
[5]Department of Histology, Faculty of Medicine, Universitas Andalas, Padang 25163, Indonesia

Corresponding Author: dr. Efrida
Department of Clinical Pathology and Laboratory Medicine, Faculty of Medicine, Universitas Andalas, Padang, Indonesia
Tel.: (+6281266582970)
Email: efrida@med.unand.ac.id

DECLARATION

Acknowledgments: Not applicable.

Generative AI and AI-assisted technologies: AI-assisted tools were used solely for language editing and grammar improvement. All scientific content, interpretation, and conclusions remain the responsibility of the authors.

Ethical approval: Ethical approval was obtained from the Ethics and Research Committee of the Faculty of Medicine, Universitas Riau, Pekanbaru, Indonesia (No. B/068/UN19.5.1.1.8/UEPKK/2024). All procedures were conducted in accordance with the Declaration of Helsinki.

Consent to participate: Written informed consent was obtained from all participants prior to enrollment in the study.

Consent for publication: All authors have reviewed and approved the final version of the manuscript for publication.

Authors' contributions: JO: conceptual, data curation, formal analysis, methodology, writing; EF: investigation, project administration, resources, supervision; MB: software, validation, supervision, writing; ED: visualisation, validation, supervision.

Data availability: The data supporting the findings of this study are available within the article. Additional data may be obtained from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

Funding: This research received no external funding.

No financial support: This research received no external funding.

Supplementary information: Not applicable.

ABSTRACT

Background: Lung cancer remains a leading cause of cancer-related mortality worldwide. Perioperative factors, including anesthetic techniques, may influence tumor biology by modulating inflammatory and angiogenic mediators. VEGF, TGF-β, and IL-6 are key regulators of tumor progression and immune response; however, evidence regarding the effects of anesthetic modalities on these biomarkers during diagnostic bronchoscopy remains limited.

Methods: This analytical observational study included 40 lung cancer patients undergoing diagnostic bronchoscopy under general anesthesia. Patients were assigned to inhalational anesthesia with sevoflurane (n = 20) or intravenous anesthesia with propofol (n = 20). Serum VEGF, TGF-β, and IL-6 levels were measured before bronchoscopy and 24 hours post-procedure using ELISA. Statistical significance was defined as $p < 0.05$.

Results: Serum VEGF levels increased significantly following bronchoscopy under general anesthesia. Both groups demonstrated postoperative elevations in angiogenic and inflammatory biomarkers. Although VEGF levels rose more prominently in the sevoflurane group than in the propofol group, the difference was not statistically significant. Similar patterns were observed for TGF-β and IL-6.

Conclusion: General anesthesia combined with bronchoscopy is associated with significant perioperative increases in angiogenic and inflammatory biomarkers in lung cancer patients. While sevoflurane tended to produce higher VEGF elevations than propofol, no significant intergroup differences were identified. These findings suggest that perioperative biological responses occur regardless of anesthetic modality, although the potential pro-angiogenic profile of volatile anesthetics warrants further investigation in larger controlled studies.

KEYWORDS: Lung Neoplasms; Propofol; Sevoflurane; Bronchoscopy; Angiogenesis.

How to cite this article: Johannas, Efrida, Basyar M, Darwin E. Perioperative Angiogenic and Inflammatory Biomarker

RESEARCH PAPER
Responses to Sevoflurane and Propofol in Lung Cancer Patients Undergoing Diagnostic Bronchoscopy. Int J Drug Deliv Technol. 2026;16(52s): 939-944. DOI: 10.25258/ijddt.16.52s.118
Source of support: Nil.
Conflict of interest: None
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1. INTRODUCTION

Lung cancer remains one of the leading causes of cancer-related mortality worldwide[1,2] and continues to impose a substantial global health burden despite advances in diagnostic and therapeutic strategies. The high mortality rate is largely attributable to late-stage diagnosis and aggressive tumor biology, with many patients presenting at advanced stages of disease. Tumor progression and metastasis are complex processes influenced not only by intrinsic tumor characteristics but also by perioperative factors related to diagnostic and therapeutic interventions.

Angiogenesis and inflammation play central roles in lung cancer development and progression[3,4]. Vascular endothelial growth factor (VEGF) is a key mediator of tumor angiogenesis, promoting endothelial cell proliferation, vascular permeability, and neovascular formation. Elevated VEGF expression has been consistently associated with advanced disease stage, increased metastatic potential, and poor prognosis in lung cancer patients[4,5]. In addition to VEGF, inflammatory cytokines such as transforming growth factor-beta (TGF-β) and interleukin-6 (IL-6) contribute to tumor progression[6,7] by facilitating immune suppression, epithelial–mesenchymal transition, and tumor cell survival within the tumor microenvironment.

Perioperative stress responses, including tissue manipulation, hypoxia, and systemic inflammation, have been shown to activate angiogenic and inflammatory pathways. Surgical procedures and diagnostic interventions may therefore transiently enhance the release of pro-angiogenic and pro-inflammatory mediators, potentially influencing tumor behavior. Increasing evidence suggests that anesthetic agents themselves may further modulate these biological responses[8–10]. Inhalational anesthetics, such as sevoflurane, have been reported to activate hypoxia-inducible factor–dependent pathways and increase VEGF expression, thereby promoting angiogenic signaling. In contrast, intravenous anesthetic agents such as propofol have demonstrated anti-inflammatory and anti-angiogenic effects in both experimental and clinical studies, including suppression of VEGF and TGF-β–related pathways[11–13].

Previous clinical investigations have explored the impact of anesthetic techniques on perioperative cytokine responses and oncologic outcomes in various malignancies. However, findings remain inconsistent, and data specific to lung cancer—particularly in the context of diagnostic bronchoscopy—are limited[14,15]. Bronchoscopy, although minimally invasive, involves direct airway manipulation and tumor contact[16,17], which may trigger inflammatory and angiogenic responses, especially in patients with advanced disease.

Given the potential influence of anesthetic technique on perioperative tumor-related pathways, further evaluation in lung cancer patients is clinically relevant. Therefore, this study aimed to compare the effects of inhalational anesthesia using sevoflurane and intravenous anesthesia using propofol on serum levels of VEGF, TGF-β, and IL-6 in lung cancer patients undergoing diagnostic bronchoscopy. Understanding these perioperative biological changes may provide insight into the role of anesthetic selection in modulating inflammatory and angiogenic responses in oncologic patients.

2. MATERIALS AND METHODS.

This prospective analytical observational study was conducted in patients with lung cancer who underwent diagnostic bronchoscopy under general anesthesia at Arifin Achmad General Hospital, Pekanbaru, Indonesia, between June and September 2024. Consecutive patients who met the eligibility criteria were recruited after providing written informed consent.

Eligible participants were adults aged 18–70 years with an American Society of Anesthesiologists (ASA) physical status classification of I–III. Patients with severe cardiac disease, clinically significant arrhythmias, or those who declined participation were excluded. A total of 40 patients were enrolled following sample size calculation with an anticipated dropout rate of 10%.

Participants were allocated into two groups based on the anesthetic technique administered during bronchoscopy. The choice of anesthetic technique was determined by the attending anesthesiologist according to clinical considerations. Twenty patients received inhalational anesthesia with sevoflurane, while twenty patients received intravenous anesthesia with propofol. All enrolled patients completed the study and were included in the final analysis.

Venous blood samples were collected under aseptic conditions into serum tubes at two time points: two hours prior to bronchoscopy and 24 hours after the procedure. Samples were labeled, stored at −20°C, and transported to the Clinical Pathology Laboratory under controlled conditions. Serum was separated by centrifugation at 3000 rpm for 10 minutes prior to analysis.

Serum levels of vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-β), and interleukin-6 (IL-6) were measured using enzyme-linked immunosorbent assay (ELISA) kits in accordance with the manufacturer's protocol. All biomarker concentrations were expressed in pg/mL. The depth of anesthesia was monitored intraoperatively using bispectral index monitoring to ensure adequate anesthetic depth in both groups.

Statistical analyses were performed using appropriate statistical software. Descriptive statistics were used to summarize baseline characteristics. Continuous variables were presented as mean ± standard deviation or median with ranges, depending on data distribution. Within-group comparisons were analyzed using paired t-tests for normally distributed data or Wilcoxon signed-rank tests for non-normal distributions. Between-group comparisons were conducted using independent statistical tests as appropriate. A p-value < 0.05 was considered statistically significant.

The study protocol was approved by the Ethics and Research Committee of the Faculty of Medicine, Universitas Riau (No. B/068/UN19.5.1.1.8/UEPKK/2024), with institutional permission granted by Arifin Achmad General Hospital, Pekanbaru. All procedures were performed in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants prior to enrollment.

3. RESULTS

Following sample size calculation and adjustment for potential dropout, 40 patients were enrolled in the study. Participants were divided into two groups: 20 patients received inhalational anesthesia with sevoflurane, and 20 patients received intravenous anesthesia with propofol. Baseline characteristics of the study subjects are presented in Table 1.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Participants

Characteristics	Sevoflurane Group (n = 20)	Propofol Group (n = 20)	p-value
Age (years)	56.75 (8.96)	55.80 (9.31)	0.744
Body weight (kg)	49.9 (8.14)	58.65 (12.65)	0.013
Height (cm)	162.5 (0.26)	162.75 (0.26)	0.759
Body mass index (kg/m²)	18.93 (3.25)	22.16 (4.82)	0.018

Table 1. (continued) Baseline Demographic and Clinical Characteristics of the Study Participants

Characteristics	Sevoflurane Group (n = 20)	Propofol Group (n = 20)	p-value
ASA physical status, n (%)			
I	-	-	
II	10 (50%)	7 (35%)	
III	10 (50%)	13 (65%)	
Tumor stage (TNM), n (%)			
Stage I	-	-	
Stage II	-	-	
Stage III	3 (15%)	1 (5%)	
Stage IV	17(85%)	19 (95%)	
Duration of anesthesia (min)	32. (5.48)	34.50 (4.84)	0.427
Systolic blood pressure (mmHg)	115.10 (15.18)	110.65 (19.82)	0.430
Diastolic blood pressure (mmHg)	70.10 (8.81)	68.45 (12.48)	0.632
Mean arterial pressure (mmHg)	88.30 (7.23)	85.25 (14.14)	0.396
Heart rate (beats/min)	89.20 (15.89)	92.70 (11.30)	0.427

Data are presented as mean (SD) or n (%).

Comparisons between groups were performed using the independent t-test or Mann–Whitney U test, as appropriate.

Categorical variables were analyzed using the chi-square test or Fisher's exact test.

A p-value < 0.05 was considered statistically significant.

Serum levels of vascular endothelial growth factor (VEGF), transforming growth factor-beta (TGF-β), and interleukin-6 (IL-6) were measured before bronchoscopy and 24 hours after the procedure. Perioperative changes in biomarker levels are summarized in Table 2. A significant postoperative increase was observed in TGF-β and IL-6 levels following bronchoscopy.

Table 2. Perioperative Changes in Angiogenic and Inflammatory Biomarkers Following Diagnostic Bronchoscopy

	Before	After	Pre - post	P value
TGF B (pg/mL)	405.27± (120.20 – 2049.10)	569.55± (145.58-2139.94)	96.63± (-31.49-659.05)	0.00
IL6 (pg/mL)	11.62± (1.85-82.30)	16.35± (2.85-95.77)	4.43± (-45.69-45.82)	0.01

As shown in Table 3, patients in the sevoflurane group exhibited a greater postoperative increase in VEGF levels compared with those in the propofol group; however, the difference between anesthetic techniques did not reach statistical significance.

Table 3. Comparison of Perioperative VEGF Changes Between Sevoflurane and Propofol Anesthesia

Group	TGF B levels (pg/ml)			P value
	Before	After	Pre - post	
Sevoflurane	808.26± (177.47-1555.06)	944.69± (218.19-1744.44)	109.08 ± (-31.49-432.38)	0.48
Propofol	316.18± (120.20-2049.10)	405.26± (145.58-2139.94)	92.76± (-25.89-659.05)	

Changes in IL-6 levels between anesthetic groups are presented in Table 4. Although patients receiving inhalational anesthesia tended to demonstrate higher postoperative cytokine levels, no statistically significant intergroup differences were observed.

Table 4. Comparison of Perioperative IL-6 Changes Between Sevoflurane and Propofol Anesthesia

Group	IL-6 levels (pg/ml)			P value
	Before	After	Pre - post	
Sevofluran	11.63± (1.85-41.20)	21.55± (7.18-43.65)	5.88± (-16.08-32.54)	0.15
Propofol	11.35± (12.35-82.30)	14.25± (2.85-95.77)	2.05± (-45.69-45.82)	

4. DISCUSSION

The increase in VEGF may be attributable to perioperative stress responses associated with airway manipulation and transient tissue hypoxia during bronchoscopy. VEGF is a central mediator of tumor angiogenesis and has been associated with tumor progression and unfavorable prognosis in lung cancer[4,18]. Procedural stress and systemic inflammatory responses may therefore stimulate VEGF release, potentially enhancing angiogenic signaling in the perioperative setting.

Both TGF-β and IL-6 levels increased following bronchoscopy across the two groups, suggesting that bronchoscopy performed under general anesthesia can trigger a measurable systemic inflammatory response independent of anesthetic technique.

Transforming growth factor-beta and interleukin-6 play critical roles in immune regulation, epithelial–mesenchymal transition, and tumor cell survival. The perioperative elevation of these cytokines aligns with previous evidence[10,13] indicating that surgical and diagnostic interventions may modulate tumor-related inflammatory pathways[19]. Although propofol has been reported to exhibit anti-inflammatory and anti-angiogenic properties in experimental models, the

absence of significant differences in this clinical study may be explained by the relatively short procedural duration, limited sample size, and timing of biomarker assessment[11,12].

Importantly, the lack of statistically significant differences between anesthetic techniques suggests that short-term perioperative alterations in angiogenic and inflammatory biomarkers may be driven primarily by the bronchoscopy procedure rather than the anesthetic agent itself. These findings should be interpreted cautiously, as the present study was not designed to evaluate long-term oncologic outcomes such as tumor recurrence or survival; therefore, no causal relationship between anesthetic technique and cancer progression can be established.

Several limitations warrant consideration. The relatively small sample size may have reduced the statistical power to detect subtle intergroup differences. Biomarker measurements were limited to two perioperative time points, precluding assessment of longer-term biological responses. Furthermore, tumor stage and histopathological characteristics were not analyzed in depth, which may have influenced biomarker dynamics.

Despite these limitations, this study provides clinically relevant insights into perioperative angiogenic and inflammatory responses in lung cancer patients undergoing diagnostic bronchoscopy. The findings contribute to the expanding body of literature exploring the interaction between anesthetic management and tumor biology and underscore the need for future studies with larger cohorts and extended follow-up to clarify the clinical implications of anesthetic selection in oncologic populations.

5. CONCLUSION

Diagnostic bronchoscopy under general anesthesia triggers measurable angiogenic and inflammatory responses in lung cancer patients. While sevoflurane showed a tendency toward higher postoperative biomarker levels compared with propofol, anesthetic technique was not significantly associated with differential biomarker expression. These findings suggest that perioperative biological alterations are likely influenced by procedural factors. Larger prospective studies are needed to determine whether anesthetic selection influences long-term oncologic outcomes.

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