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## Effect of Serratus Anterior Plane Block Combined with Dexmedetomidine as an Adjuvant to Ropivacaine on Inflammatory Response and Opioid Doses in Patients Undergoing Video Assisted Thoracoscopic Surgery

Afi Adi Kirana<sup>1</sup>, Philia Setiawan<sup>2\*</sup>, Herdiani Sulisyo Putri<sup>3</sup>, Christrijogo Soemartono<sup>4</sup>, Prihatma Kriswidyatomo<sup>5</sup>, Pudji Lestari<sup>6</sup>

<sup>1,2,3,4,5</sup>Department of Anesthesiology and Intensive Care, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya, Indonesia

<sup>6</sup>Department of Public Health and Preventive Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya 60115, Indonesia

Emails: <sup>2</sup>Philstawn@yahoo.com

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### ABSTRACT

**Background:** VATS has the potential of pain scale and stress response comparable to thoracotomy. The SAP block for pain management is one of alternative to thoracic epidural, but the ability to control the stress response is still underexpected. Additional dexmedetomidine to local anesthesia theoretically enhance the block's effectiveness in pain management and stress response control by reducing the inflammatory mediators.

**Aim:** This study aims to investigate the effect of combining dexmedetomidine with ropivacaine in a serratus anterior plane block (SAPB) on inflammatory response and opioid dosage in patients undergoing video-assisted thoracoscopic surgery (VATS).

**Material and Methods:** This is a double blinded, prospective analytical experimental study conducted on VATS patients Dr. Soetomo Hospital from January to March 2024. We divided 40 subjects into two groups, groups R and RD. Following anesthesia induction, The RD Group received SAP block with ropivacaine 0,375% plus adjuvant dexmedetomidine 1 mcg/kg, The R Group received SAP Block with ropivacaine 0,375%. Both diluted into 20 cc volume. We analyzed the IL-6 and NLR values before the incision, 6 hours, and 24 hours after the incision. We also analyzed the total fentanyl dose during surgery, and post operative morphine demand.

**Results:** There were no differences in demographic data between the two groups. Baseline IL-6 and NLR values also had no significant differences. At the 6th hour, the percentage increase in IL-6 was significantly lower in the RD group compared to the R group, but at the 24th hour, there was no significant difference. The NLR comparison test revealed that the RD group experienced a lower percentage increase in NLR at 6 hours after incision, but no significant difference at 24 hours. Total intraoperative fentanyl requirements and postoperative morphine demands were also significantly lower in the RD group.

**Conclusion:** Adjuvant dexmedetomidine in SAP block with local anesthetic ropivacaine may reduce the expression of stress response at 6 hours post-incision and the opioid requirement.

**Keywords:** Serratus Anterior Plane Block, Dexmedetomidine, IL-6, NLR, Fentanyl

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## 1. Introduction

Video-Assisted Thoracoscopic Surgery (VATS), like other minimally invasive technique, often performed by thoracic surgeons as a development of open thoracotomy. This technique is characterized by smaller incisions and no ribs retractors needed as in open thoracotomy. Although this technique is classified as minimally invasive, the pain that arises is said to be close to conventional techniques (Umari et al., 2018). In addition to pain, it turns out that the VATS technique also has a pattern of increased immunological stress response that is identical to the open thoracotomy technique. This inflammatory response exerts a protective effect on body function, which can become detrimental when it reaches pathological levels. The inflammatory response is initially local to the injured area, but can develop into a systemic response, and an excessive reaction can even occur resulting in systemic inflammatory response syndrome (SIRS) (Yim et al., 2000).

The use of a combination of general anesthesia combined with regional anesthesia, in addition to improving the quality and duration of analgesics, can also suppress immunological, endocrine, and metabolic responses due to surgery. Serratus Anterior Plane Block (SAPB) is an alternative technique to regional anesthesia for the thoracic area surgery, including VATS. This technique has the advantage of being relatively easy to do, safe, and have no sympathetic blockade. In terms of effectiveness in pain control, this technique comparable with thoracic epidural, intercostal, or paravertebral blocks (Cai et al., 2023; Lee & Kim, 2019; Umari et al., 2018). The analgesic effect of single shot SAP block only lasts up to 8-9 hours after injection, after which patients rely more on opioids from Patient Controlled Intravenous Analgesia (PCIA) (de Cassai et al., 2021). When viewed from the effect of controlling the surgical stress response, it turns out that SAPB is inferior to the Paravertebral Block technique (Cai et al., 2023).

Dexmedetomidine, a class of selective  $\alpha_2$ -adrenergic agonists has been widely used as a sedation drug and adjuvant in general anesthesia. Dexmedetomidine has several mechanisms that are thought to amplify the analgesia effect of local anesthetics. It has been successfully used as an adjuvant in intrathecal, epidural, and paravertebral blocks (Abdallah et al., 2019). In addition to the analgesia effect, dexmedetomidine has a suppressive effect on inflammatory mediators which is thought to be through the mechanism of inhibition of  $\alpha_2$ -adrenoceptor-mediated and necrosis factor  $\kappa$ B (NF- $\kappa$ B) (Sherif et al., 2022). Our study is aimed to assess the effect of dexmedetomidine adjuvant administration in SAPB on surgical stress response represented by two biomarkers, interleukin-6 (IL-6) and neutrophil-lymphocyte ratio (NLR). We hypothesized that adjuvant dexmedetomidine could suppress the increase in inflammatory markers IL-6 and NLR after incision, and can reduce the need for medication during and after surgery.

## 2. Methodology

This is a randomized, double-blind trial included 40 adult patients undergoing VATS in period from January to March 2024. The study was carried out at Dr. Soetomo General Hospital after approval of the local ethical committee (ethical clearance number 0900/KEPK/I/2024), and all patients have provided written informed consents to participate. Patients were given a full detailed explanation of study protocol, including the potential benefits of the succesful technique as well as the side-effects.

Inclusion criteria were 17 to 65 years old patients undergoing VATS surgery with SAPB as adjunctive regional analgesia technique and ASA status I-III. Exclusion criteria were refusal for SAPB, immunosuppressive, shock, symptomatic bradycardia, pulmonary embolism, myocardial infarct, atrial fibrillation, congestive heart failure, and chronic kidney disease above stage 3. Drop out criteria were converting surgery to open thoracotomy, using the ventilator after surgery, and have allergy reaction after the medication given. Computer-generated numbers did randomization. These codes were placed in sealed

and numbered envelopes, drawn before starting the anesthesia procedure.

**Anesthesia preparation and induction :**

Patients were fasting six hours before and stop drinking two hours before the operation. Routine preoperative preparation included electrocardiogram (ECG), heart rate (HR), oxygen saturation (SpO<sub>2</sub>). The induction of anesthesia with 2µg/kg fentanyl, 1,5mg/kg propofol, 0,8mg/kg rocuronium. A double-lumen tube with appropriate size was inserted, and mechanical ventilation was started after the position of the tube is secured by fiberoptic evaluation. Invasive blood pressure monitoring and additional extra large bore intravenous line was conducted after induction of anesthesia.

**Anesthesia maintenance :**

Anesthesia was maintained with sevoflurane or isoflurane 1 – 1,5 minimum alveolar concentration (MAC) in O<sub>2</sub> and air. The depth of anesthesia is monitored by Conox ® [target index of consciousness (qCon) 40-60], alternatively using the hemodynamic movements that occur during surgery. Relaxant rocuronium 0,4-0,6 mg/kg/hour or atracurium 0,4 mg/kg/hour. 1µg/kg fentanyl used for analgetic rescue, and ephedrine 10mg used for hemodynamic rescue if mean arterial pressure below 65.

**Analgesic methods :**

SAPB is performed after induction of anesthesia by performed by an attending anesthesiologist not involved in the research team, assisted by a senior resident. Patient is positioned in lateral decubitus, with the upper arm abducted and the elbow flexed. The high-frequency linear array ultrasound probe (Portable Sonosite ® EDGE II ultrasound) was placed and the mid axillary line, at the 4th and 5th ribs, to find the plane between serratus anterior and latissimus dorsi (superficial technique). The 25g spinal needle was advanced until it crossed the latissimus dorsi to the serratus anterior. After confirming that there is no blood return and no air, 20 ml 0,375% ropivacaine (R group), plus addition of pure 1µg/kg dexmedetomidine (RD group) were injected slowly, and the spread of local anesthetic drugs was observed directly via ultrasound. 1 gram of paracetamol were given before the surgical incision.

**End of surgery :**

Inhalation agents and muscle relaxant drugs are discontinued. Neuromuscular blockade was reversed by IV injection of neostigmine 0,05mg/kg with atropine 0,01mg/kg after fulfilling criteria of extubation. Patients were extubated then transferred to post anesthesia care unit (PACU), and monitored closely with standard monitor. For postoperative pain management, the patient was given additional analgesic ketorolac 30 mg (continued routinely every 8 hours in the initial 24 hours), paracetamol 10 mg/kg continued also every 8 hours. Rescue morphine at a dose of 0.1mg/kg is given if the NRS value is above 5.

**Basic characteristics and indexes :**

The data taken includes : intraoperative fentanyl used, serum IL-6, and NLR, and postoperative morphine given. Four milliliters of vein blood was collected and divided in non-anticoagulant tubes for complete blood count, and gel activator clot tube for IL-6 examination. Blood was centrifuged and separated from the serum (rate 3000r/minutes, duration 10 minutes). Enzyme linked immunosorbent assays (ELISA) was used to detect IL-6. Absolute neutrophil and lymphocyte counts were derived from differential percentages of leukocytes measured by automatic cell counters. Blood sampling for inflammatory biomarkers performed on pre-operatively on the morning of surgery (T1) and then at 6 h (T2) and 24 h (T3) after surgery. Complication after block were also collected and analyzed. Bradycardia and hypotension event were collected within an hour after block. PONV incident was collected start from recovery room until 24 hours post surgery. RASS below 2 were known as sedation, and collected start from recovery room until 24 hour post surgery. Those data will

be presented as secondary outcomes.

#### Statistical analysis :

Statistical analysis was performed on all collected data using SPSS 27 (SPSS Inc., Chicago, USA). The individuals demographic homogeneity was assessed. The Shapiro-Wilk test was used to determine the data normalcy. IL-6, NLR, use of fentanyl during surgery, and postoperative morphine rescue were compared between the two groups using a Mann-Whitney test if the data was not normally distributed, or a two-independent T-test if the data was normally distributed. Chi-square test and Fisher's-exact test were used for comparing the categorical data. The entire graph is depicted using GraphPad Prism 9 software (GraphPad Software Inc., San Diego, CA, USA). The categorical data are expressed as frequencies (%), and the continuous and discrete variables as mean  $\pm$  SD or median (interquartile range). A p-value  $< 0,05$  was considered statistically significant.

### 3. Results and Discussion

#### Results

The study included 40 patients in total. Both groups were homegenous in terms of equality of gender, age, body mass index (BMI), American Society of Anesthesiologist (ASA) scores, duration of surgery, duration of anesthesia, and the type of VATS surgery. The demographic characteristics of the subjects are summarized in Table 1.

**Table 1. Demographic characteristic of subjects**

Characteristics	Group R (n=20)	Group RD (n=20)	Total (n=40)	<i>p-value of Homogeneity test</i>
<b>Gender</b>				
Male	15 (75%)	15 (75%)	30 (75%)	1,00 <sup>a</sup>
Female	5 (25%)	5 (25%)	10 (25%)	
<b>Age (year)</b>				
Median	51	47	50,50	1,00 <sup>b</sup>
(min – max)	(18-65)	(18-65)	(18-65)	
<b>BMI</b>				
Mean $\pm$ SD	22,250 $\pm$ 4,19	20,86 $\pm$ 4,21	22,02 $\pm$ 1,98	0,31 <sup>c</sup>
<b>ASA</b>				
1	1 (5%)	0 (0%)	1 (2,5%)	0,42 <sup>d</sup>
2	12 (60%)	10 (50%)	22 (55%)	
3	7 (35%)	10 (50%)	17 (42,5%)	
<b>Duration of Surgery (Minutes)</b>				
Mean $\pm$ SD	99,25 $\pm$ 22,02	92 $\pm$ 19,36	95,63 $\pm$ 20,79	0,28 <sup>c</sup>
<b>Duration of Anesthesia (Minutes)</b>				
Mean $\pm$ SD	153,25 $\pm$ 21,17	145 $\pm$ 18,57	149,12 $\pm$ 20,09	0,20 <sup>c</sup>
<b>Type of VATS</b>				
Sympathectomy	1 (5%)	1 (5%)	2 (5%)	1,00 <sup>d</sup>
Decortication	4 (20%)	5 (25%)	9 (22,5%)	
BPF Repair	5 (25%)	5 (25%)	10 (25%)	
Wedge Resection	3 (15%)	2 (5%)	5 (12,5%)	
Open Biopsy	4 (20%)	5 (25%)	9 (22,5%)	
Tumor Excision	3 (15%)	2 (10%)	5 (12,5%)	

Data are presented as median (min-max), mean  $\pm$  SD, or number (percentage)

<sup>a</sup> Chi square test

<sup>b</sup> Mann-Whitney U

<sup>c</sup> Independent T-Test

<sup>d</sup> Fisher's Exact test

**Table 2. Inflammatory Biomarkers**

Time	Group R (n=20)	Group RD (n=20)	<i>p-value</i>
IL-6 (pg/ml)			
T <sub>0</sub>	46,30 ± 11,45	47,56 ± 14,66	0,75 <sub>a</sub>
T <sub>1</sub>	62,68 (39,57 – 100,63)	57,23 (33,86 – 107,44)	0,21 <sub>b</sub>
T <sub>2</sub>	54,85 ± 20,26	60,40 ± 24,59	0,43 <sub>a</sub>
ΔIL-6 (%)			
Δ1	42,53 ± 20,54	24,50 ± 14,10	<0,01 <sub>a</sub>
Δ2	19,11 (-32,02 – 86,58)	25,02 (-38,17 – 242,53)	0,60 <sub>b</sub>
NLR			
T <sub>0</sub>	3,55 ± 1,80	3,40 ± 1,52	0,75 <sub>b</sub>
T <sub>1</sub>	17,80 (7,8 – 30)	13,00 (6,4 – 26,0)	<0,01 <sub>a</sub>
T <sub>2</sub>	8,55 (4,5 – 13,1)	7,50 (2,5 – 16,4)	0,47 <sub>a</sub>
ΔNLR (%)			
Δ1	504,59 (80,95 – 1644,44)	287,11 (17,74 – 1030,43)	0,04 <sub>a</sub>
Δ2	160,03 (-12,7 – 773,3)	105,79 (-3,23 – 613,04)	0,56 <sub>a</sub>

Data are presented as median (min-max) or mean ± SD

T<sub>0</sub> : Before incision

T<sub>1</sub> : 6 hours after incision

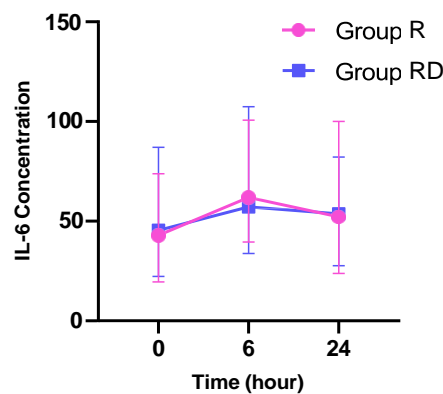
T<sub>2</sub> : 24 hours after incision

Δ1 : Delta (difference) pre incision to 6 hour after incision in percentage

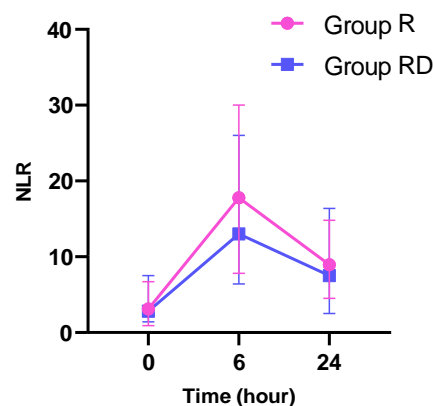
Δ2 : Delta (difference) pre incision to 24 hour after incision in percentage

a Mann-Whitney U

b Independent T-test



**Figure 1. Comparison of changes in interleukin-6 (IL-6) levels in the group that received dexmedetomidine adjuvant (Group RD) and the ropivacaine group (Group R). The RD group had lower percentage increases in IL-6 levels at hour 6 ( $p < 0,01$ ), but not significantly at hour 24 ( $p = 0,56$ ).**



**Figure 2. Comparison of changes in neutrophil-lymphocytes ratio (NLR) levels in the group that received dexmedetomidine adjuvant (Group RD) and the ropivacaine group (Group R). The RD group had lower percentage increases in NLR levels at hour 6 ( $p = 0,04$ ), but not significantly at hour 24 ( $p = 0,60$ ).**

There was no significant difference in absolute IL-6 levels between the two groups at pre-incision, 6 hours post-incision, or 24 hours post-incision. However, when viewed from the percentage change in IL-6 from the baseline value, the RD group had a smaller increase than the R group at 6 hours post-incision ( $p < 0.01$ ), but at 24 hours post-incision there was no significant difference between the two groups ( $p = 0.56$ ). In the NLR examination, there was no significant difference in the baseline NLR value. At 6 hours post-incision, the absolute value of NLR in the RD group was lower than the R group ( $p < 0.05$ ). In the assessment at 24 hours post-incision, the absolute value of NLR in both groups was not significantly different ( $p = 0.04$ ). In terms of changes in NLR, it was found that at 6 hours post-incision, the RD group had a smaller increase in NLR value than the R group ( $p = 0.04$ ), but at 24 hours there was no significant change ( $p = 0.60$ ).

**Table 3. Opioid consumption**

	Group R (n=20)	Group RD (n=20)	<i>p-value</i>
Intraoperative fentanyl	2,10 (1,3 - 2,7)	1,50 (1,1 - 2,5)	0,04 <sub>a</sub>
Postoperative morphine rescue n (%)			
Yes	9 (45)	2 (10)	0,02 <sub>b</sub>
No	11 (55)	18 (90)	
Timing of morphine administration (hour)	17,22 ± 3,31	22,5 ± 0,71	0,04 <sub>c</sub>

Data are presented as median (min-max), mean ± SD, or number (percentage)

a Mann-Whitney U

b Fisher's Exact

c Independent T-Test

Either the use of intraoperative fentanyl or postoperative morphine demand in the RD group was less than the R group ( $p = 0,04$  and  $0,02$  respectively).

In the data collection of complications of bradycardia and hypotension within 1 hour after SAPB, and the incidence of PONV and decreased consciousness for 24 hours after surgery, there is no significant difference between the two groups.

**Table 4. Secondary Outcome (Complication)**

	Group R (n=20)	Group RD (n=20)	<i>p-value</i>
<b>Bradycardia</b>			
Yes	0 (0%)	3 (18%)	0,23 <sub>a</sub>
No	20 (100%)	17 (82%)	
<b>Hypotension</b>			
Yes	1 (5%)	2 (10%)	1,00 <sub>a</sub>
No	19 (95%)	18 (90%)	
<b>PONV</b>			
Yes	5 (25%)	2 (10%)	0,41 <sub>a</sub>
No	15 (75%)	18 (90%)	
<b>Sedation</b>			
Yes	0 (0%)	0 (0%)	-
No	20 (100%)	20 (100%)	

Data are presented as median (min-max), mean  $\pm$  SD, or number (percentage)

<sub>a</sub> Fisher's Exact

## Discussion

Cytokines play a central role in the body's changes in response to stress. Activation of a wide range of cytokines is a response to trauma resulting from surgery and anesthesia. Interleukin-6 is released as the "second wave" of cytokines and acts also as the most important effector of protein production in the acute phase and other inflammatory cells. Elevation of IL-6 in major surgeries reflect advanced tissue damage, and are associated with patient outcomes (Garcia et al., 2002). IL-6 concentrations in the blood begin to rise 1 hour after the start of surgical incision, reach a peak at 24 hours post-incision, and begin to fall after 24 hours post-surgery, provided there are no infectious complications, excessive drain production or bleeding in the post-surgical period (Sakamoto et al., 1994). Interleukin-6 is part of a wide range of cytokines released by immune cells and is suspected to trigger intense hyperalgesia. So far there is no clear evidence that cytokines directly affect the excitability of sensory nerve fibers, but it is suspected that the activation of vagal afferents and cutaneous nerves may be affected by these cytokines. The process of hyperalgesia caused by cytokine release needs to be further investigated, as well as its relationship with neurocircuitries and neurochemistries (Nagahiro et al., 2001).

Neutrophil-lymphocyte ratio (NLR) is known to have a significant association with the outcome or prognosis of various clinical conditions including surgical stimulus (Ülger et al., 2022). NLR can also be used as a predictive tool for postoperative pain through inflammatory pathways that are the effects of trauma or surgery (Ülger et al., 2022). The inflammatory response in the surgical area is also responsible for nociceptor sensitivity and hyperalgesia. NLR has several advantages when used as an indicator of systemic inflammation in patients. The first advantage is that it is easy to calculate and inexpensive because NLR is derived from a complete blood test that has been routinely performed in the perioperative process. The next advantage is that the examination is easy because it can be obtained from peripheral blood examination. NLR examination can be observed repeatedly in cases that require periodic monitoring of inflammatory markers (Ülger et al., 2022).

Dexmedetomidine is generally known to have several anti-inflammatory mechanisms. This theory is still being extensively studied. Some theories of the anti-inflammatory mechanism of dexmedetomidine are : regulation of cytokines produced by immune cells, direct effect as an antinociceptive, redirection of the cholinergic anti-inflammatory pathway through central sympatholytics (Du et al., 2021). By inhibiting adrenergic tone in effector tissues, dexmedetomidine can play a role in modulating cytokine production through lymphocytes, macrophages, and monocytes during the body's response to stress, this leads to suppression of proinflammatory cytokines such as IL-6, IL-8, and TNF-alpha in serum up to 24 hours postoperatively (Kawasaki et al., 2013).

In this study, there was a significant difference in the percentage change in IL-6 increase at the 6th hour after incision, but at the 24th hour there was no significant difference. There are still not many studies on the effects of dexmedetomidine given as an

adjuvant of local anesthesia and associated with the expression of inflammatory marker release. In a study on the adjuvant effect of dexmedetomidine administered with local anesthetic bupivacaine on wound infiltration after hysterectomy, it was found that the group given dexmedetomidine adjuvant produced lower levels of pro-inflammatory biomarkers such as IL-6, IL-10, and TNF-alpha at 6 hours and 24 hours postoperatively when compared to the control group (pure bupivacaine) (Sherif et al., 2022). Another study on the effects of dexmedetomidine administered locally (intra-articular) compared with intrathecal injection and placebo in patients undergoing knee arthroscopy, found that intra-arterial administration was better at suppressing the increase in serum C-reactive protein compared with intrathecal administration and placebo (Ismail et al., 2017). There are no studies that state how long the definite effect of adjuvant dexmedetomidine is in suppressing the release of the inflammatory response. We think that basically dexmedetomidine is a drug that has a fairly short duration of action, so that single shot administration only has an effect for 6 hours (in suppressing pro-inflammatory cytokines) as we found in this study.

There are several theories regarding the effect of dexmedetomidine as a local anesthetic adjuvant and its role in helping to regulate the surgical stress response. The first opinion is that dexmedetomidine can suppress inflammatory mediators through  $\alpha_2$ -adrenoceptor-mediated mechanisms and necrosis factor- $\kappa$ B (NF- $\kappa$ B) at peripheral receptors. These mechanisms are responsible for the decreased production of TNF- $\alpha$  and IL-6. Dexmedetomidine is also known to suppress the sympathetic response and stimulate the parasympathetic system. Stimulation of the vagus nerve has anti-inflammatory effects by suppressing peripheral cytokine release through macrophage nicotinic receptors and cholinergic anti-inflammatory pathways (Kawasaki et al., 2013). The next theory is the control of surgical stress response by amplifying the local direct effect of anesthesia which is known to have an effect on the regulation of proinflammatory cytokines in PMN. The synergistic effect of dexmedetomidine on local anesthesia is to maintain the hyperpolarization phase of the cell by inhibiting the activation of the H current that plays an important role in cell excitability, maintaining the depolarization of the cell, and increasing the inhibition of sodium channels so that the effect of local anesthesia can be strengthened and prolonged (B. S. Chen et al., 2009; Desiree et al., 2024; Marhofer et al., 2013).

There was a difference in the absolute value of NLR at 6 hours post-incision. There was also a difference in the percentage increase in NLR value at 6 hours post-incision, but not at 24 hours. There is still no study linking the effect of adjuvant dexmedetomidine in local anesthesia on postoperative NLR values. Systemic administration of dexmedetomidine adjuvant has several different NLR inflammatory response control outcomes. According to a study by Cho et al, systemic (intra-venous) administration of dexmedetomidine adjuvant in uterine cancer surgery patients had no effect on suppressing NLR values at periodic postoperative examinations (Cho et al., 2021). In line with the results of this study, another study states that the administration of dexmedetomidine as a general anesthetic adjuvant in laparoscopic gastrectomy surgery also does not make a significant difference regarding NLR suppression, but has the effect of suppressing pro-inflammatory cytokine IL-6 at a certain time (Moon et al., 2023). Different results were obtained in a study by Zen Du and colleagues, giving dexmedetomidine as premedication in children with one day care hernia surgery resulted in lower NLR values compared to the group given midazolam premedication and the control group (Du et al., 2021).

Surgery and anesthesia activate the neuro-endocrine system, which results in the release of hormones and cytokines. Pain in the perioperative period is described as a nociceptive, neuropathic and inflammatory stimulant associated with the stress response to surgery. In the surgical process, there are also changes in systemic leukocytes such as leukocytosis, lymphopenia, and neutrophilia (Surhonne et al., 2019). Currently, NLR has been widely used in various medical disciplines, and is considered a marker of immune response to non-infectious stimuli (Kriplani et al., 2022). NLR is not only affected by surgery, but can also be affected by the anesthesia method (Domagalska et al., 2023; Surhonne et al., 2019)). However, there are limited studies linking anesthesia method and NLR. A study from Boruah et al on the effect of anesthesia techniques on NLR values in non-cardiac surgery. In this



study, general anesthesia, total intra venous anesthesia (TIVA), and combined spinal epidural (CSE) techniques were compared, the results showed that the CSE regional anesthesia technique had a lower NLR value than general anesthesia and TIVA techniques (Boruah et al., 2023). In a study mentioned that the administration of dexmedetomidine can suppress the phagocytic activity of human neutrophils, which is associated with impaired respiration due to increased nitric oxide levels (S. L. Chen et al., 2016). However, in another study it was stated that in vitro dexmedetomidine had no effect on neutrophil or lymphocyte function (Du et al., 2021).

In addition to its effect on controlling the surgical stress response, dexmedetomidine adjuvant administration has a synergistic effect with local anesthetics (Bao et al., 2022). Dexmedetomidine is reported to prolong the duration of local anesthetic drugs in peripheral nerve blocks with either peripheral or systemic administration. The specific mechanism is still unknown. There are several theories of how dexmedetomidine works in the periphery, including central analgesia mechanisms, vasoconstrictive effects of  $\alpha_2$ -adrenoreceptors, inhibiting inflammatory responses, and direct mechanisms to peripheral nerves by blocking hyperpolarization-activated cation (Ih) which has an important role in cell excitability when blocked, Ih currents will increase hyperpolarization and inhibit action potentials (Bao et al., 2022). The administration of dexmedetomidine as a local anesthetic adjuvant to the ulnar nerve block showed a similar sensory onset time, but the duration of the block increased by 60% compared to the control group. Whereas in the systemic administration of dexmedetomidine, the sensory effect of ulnar nerve block only extends 10% (Marhofer et al., 2013). In this study, it was found that the administration of dexmedetomidine as an adjuvant can reduce the need for intraoperative fentanyl opioids and reduce the need for rescue morphine in the postoperative period.

A study examining the neurotoxicity effects of dexmedetomidine in experimental animals has been conducted, the sciatic block was given a high dose of dexmedetomidine (20-40mcg/kg) combined with ropivacaine or bupivacaine. Neurotoxicity, damage to sheaths of axons, myelin did not occur until 14 days post injection (Z. Chen et al., 2023). In another study dexmedetomidine can reduce the toxicity effect of bupivacaine by reducing cell degranulation (Tüfek et al., 2013). In addition, in a study on the administration of dexmedetomidine as an adjuvant to ropivacaine in sciatic nerve block in rats, it was found that dexmedetomidine not only prolongs sensory or motor block, but can also reduce toxicity triggered by ropivacaine, by reducing caspase-3-dependent apoptosis in the sciatic nerve (Xue et al., 2020).

Common side effects of dexmedetomidine are bradycardia, hypotension, and mild to moderate sedation. In perineural administration, dexmedetomidine can also cause side effects of bradycardia and hypotension, but it is dose dependent. In perineural administration of 50-60mcg dexmedetomidine does not cause side effects such as decreased hemodynamics and sedation (Liu et al., 2022). In this study, with a dexmedetomidine adjuvant dose of 1mcg/kg, there was no significant difference in the incidence of complications between the two groups.

In this study, the movement of inflammatory markers was only seen at the 6th and 24th hours after surgery, even though the movement of inflammatory markers due to surgery and anesthesia can last for a longer period. In this study, the relationship between patient diagnosis and inflammatory markers and opioid requirements was not examined. Not all patients use the Conox device to determine the depth of anesthesia (some use markers of hemodynamic changes), this can cause bias.

#### 4. Conclusion

The administration of dexmedetomidine as a local anesthetic adjuvant in SAPB can suppress the increase in surgical stress response at 6 hours post-incision, and can reduce the need for opioids during VATS and postoperatively.

#### Conflict of Interest

The authors affirmed that there were no conflicts of interest in this study.

### Funding

The authors were responsible for all research funding without obtaining financial support.

### Ethical Clearance

This study has obtained ethical clearance from the Research Ethics Committee of Dr. Soetomo Hospital Surabaya with reference letter number 0900/KEPK/I/2024

### Author Contribution

All authors contributed equally in this research and publication of this manuscript.

### 5. References

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