Original Article

Effects of Thoracic Epidural or Intravenous Analgesia on the Neutrophil-to-lymphocyte ratio in Thoracotomy Cases

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Abstract

Background and Purpose: Postoperative pain is a significant problem in thoracotomy patients. Our aim in this study was to investigate the relationship between postoperative pain and neutrophil-to-lymphocyte ratio (NLR) which is a marker of acute inflammatory response. **Materials and Methods:** Thoracic epidural or intravenous analgesia was administered to thoracotomy patients who elected to undergo a planned surgery. Patients were divided into two groups according to the analgesia method applied postoperatively. Thoracic epidural analgesia was recorded as Group 1 and intravenous analgesia as Group 2. Whole blood counts were recorded from preoperative and postoperative 24th- and 48th-hour routine blood samples, and NLRs were recorded as retrospective file scanning. Postoperative 24th- and 48th-hour NLRs and preoperative NLR values were recorded. **Results:** Demographic data of the patients included in the study were similar except for age. Preoperative NLR was significantly higher in Group 1 at 3.50 (P = 0.004) than in Group 2 at 2.51. Postoperative NLRs were similar among both groups. Postoperative NLR values at both the 24th- and 48th-hour increased by4.9 times in Group 1 and 9.23 times in Group 2 from the 24th-hour preoperative period, when the preoperative NLRs were evaluated. The rate of increase in Group 1 was significantly lower than in Group 2 (P = 0.006). **Conclusion:** Postoperative NLR alterations when compared with preoperative values were related to the analgesic regimen used.

Keywords: *Neutrophil-to-lymphocyte ratio, thoracic epidural, thoracotomy*

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Introduction

Thoracotomy interventions result in moderate-to-severe postoperative pain, potentially generating chronic pain development, which leads to prolonged healing processes that impair respiratory functions.[1] Uncontrolled postoperative pain increases both morbidity and hospital costs. Although thoracic epidural analgesia (TEA) is the most commonly used and most effective regional anesthetic method for the treatment of pain after thoracic surgery, parenteral opioid administration is often used effectively. However, TEA is known to be a superior method for both pain control and postoperative complications when compared with parenteral opioids.[2] Therefore, it is important to determine the selected method and effectiveness of the method. The neutrophil-to-lymphocyte ratio (NLR), a marker of inflammation, has been frequently used in mortality, morbidity, and prognostic studies in recent years because it is simple, inexpensive, and easily applicable.[3-5] Its use has also increased because the ratio is easy to calculate and is a noninvasive marker. However, there are insufficient data on the effects of postoperative pain related to acute inflammation. In this study, we aim to determine the relationship between NLR and analgesic methods used during the first 48 h in post-thoracotomy patients.

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Materials and Methods

After approval from the Ethics Committee of Gazi University Faculty of Medicine, 100 patients who underwent open thoracotomy between January 2015 and January 2017 were retrospectively screened from the file records of the patients. American Society of Anesthesiologists (ASA) I/II/III patients who underwent elective open thoracotomy and received postoperative analgesia either by thoracic epidural or intravenous route were included in the study. Patients who needed emergency surgery were excluded from the study. Patients' age, gender, ASA scores, and lung mass presence were recorded.

NLRs were obtained from routine preoperative and postoperative 24th- and 48th-hour blood samples of the patients, which were found in patient files. Postoperative 24th- and 48th-hour NLRs and preoperative NLR values were recorded. Patients were divided into two groups according to the analgesia method applied postoperatively. Group 1 patients received TEA, and Group 2 patients received IV morphine analgesia. Patient-controlled epidural analgesia is administered with epidural morphine + bupivacaine, which is the routine analgesia protocol of our clinic. Independent of the applied analgesic technique, patients received additional analgesic doses at 2 h, 1 day, and 2 days, postoperatively.

Statistical analysis

SPSS version 20.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. *P* values <0.05 were considered significant. The results of the study were expressed as mean ± standard deviation, *n* (%). Demographic data and NLR between the groups were analyzed using Student's *t*-test. Gender, ASA, and the number of patients between the groups requiring supplemental analgesics at 2, 24, and 48 h were analyzed with Fisher's test and χ^2 test. Multivariate relationship with NLR was assessed by logistic regression analysis. The correlation between NLR, age, and postoperative analgesic consumption was assessed by Spearman's correlation analysis.

Results

Demographic data of the patients included in the study were similar except for age [Table 1]. Patients were significantly older in Group 1 than Group 2 ($P < 0.0001$). The percentage of patients who underwent mass operation in lung mass was significantly higher in Group 1 (56% versus 30%, $P < 0.003$).

Preoperative NLR was significantly higher in Group 1 at 3.50 ($P = 0.004$) than in Group 2 at 2.51 [Table 2].

Table 1: Demographic data [mean±SD, *n* (%)]

	Group 1 (*n*=50)	Group 2 (*n*=50)	*P*
Age (years)	59.7±2.3	48.5±1.9*	<0.0001
Gender (M/F)	40 (80)/10 (20)	34 (68)/16 (32)	0.099
ASA (I/II/III)	3 (6)/30 (60)/17 (34)	6 (12)/36 (72)/8 (16)	0.058
Lung mass	28 (56)	15 (30)*	0.003
CRP (mg/L)	6.4±4.73	6.1±3.9	0.310
ESR (mm/h)	4.4±2.4	4.2±2.2	0.735

SD=Standard deviation; ASA=American Society of Anesthesiologists; CRP=C-reactive protein; ESR=Erythrocyte sedimentation rate. *P<0.05: compared with Group 1

Table 2: NLR rates (mean±SD)

	Group 1 (*n*=50)	Group 2 (*n*=50)	*P*
Preoperative	3.5±0.3	2.5±0.3*	0.004
Postoperative, Day 1	12.1±1.1	14.9±2.5	0.587
Postoperative, Day 2	7.8±0.6	7.4±0.9	0.748
Postoperative Day 1/preoperative	4.9±0.8	9.2±3.1*	0.006
Postoperative Day 2/preoperative	2.7±0.2	4.4±1.1	0.122

NLR=Neutrophil-to-lymphocyte ratio; SD=Standard deviation. *P<0.05: compared with Group 1

Postoperative 24th- and 48th-hour NLRs were similar among both groups. Postoperative NLR values at both the 24th- and 48th-hour increased by 4.9 times in Group 1 and 9.23 times in Group 2 from the 24th-hour preoperative period, when the preoperative NLR values were evaluated. The rate of increase in Group 1 was significantly lower than in Group 2 ($P = 0.006$).

When the data related to the use of additional analgesic were examined, additional analgesic was required by 40% of the patients in Group 1, postoperatively, at the second hour. Additional analgesic was required by100% of the patients in Group 2 [Table 3] and was significantly higher in Group 2 ($P < 0.0001$) than in Group 1.

Postoperative Day 1: 20% of Group 1 patients needed additional analgesic twice daily, whereas 90% of Group 2 patients needed additional analgesic twice daily. Group 2 patients requiring additional analgesic was significantly higher ($P < 0.0001$).

Postoperative Day 2: 60% of Group 1 patients needed additional analgesic twice daily, whereas 90% of Group 2 patients required additional analgesic twice daily. The number of Group 2 patients requiring additional analgesics twice daily was significantly higher ($P = 0.002$) [Table 3].

A very variable logistic regression analysis of the relationship between NLR and analgesic consumption in the postoperative period is shown in Table 4. The correlation between NLR and analgesic consumption in age and postoperative period is shown in Table 5. In

Table 3: Additional analgesic requirement (*n*)

	Group 1 (*n*=50)	Group 2 (*n*=50)	*P*
Postoperative Hour 2 (none/1 times/2 times)	30 (60)/20 (40)/0 (0)	0 (0)/10 (20)/35 (70)*	<0.0001
Postoperative Day 1 (none/1 times/2 times)	0 (0)/40 (80)/10 (20)	0 (0)/5 (10)/45 (90)*	<0.0001
Postoperative Day 2 (none/1 times/2 times)	5 (10)/15 (30)/30 (60)	0 (0)/5 (10)/45 (90)*	0.002

*P<0.05: compared with Group 1

Table 4: Regression analysis of some parameters with log NLR

Paramaters	β	*P*	95% CI
Age	0.014	0.454	0.977-1.054
ASA	0.288	0.400	0.230-1.245
Postoperative Hour 2 (none/1 times/2 times)	4.232	<0.0011	12.066-392.656
Postoperative Day 1 (none/1 times/2 times)	3.584	<0.0011	11.343-114.256
Postoperative Day 2 (none/1 times/2 times)	1.662	0.001	1.912-14.553

NLR=Neutrophil-to-lymphocyte ratio; CI=Confidence interval; ASA=American Society of Anesthesiologists

Table 5: Correlation between NLR, age, and additional analgesic requirement

	Group 1 (*n*=50)	Group 2 (*n*=50)
Postoperative Hour 2 (none/1 times/2 times)	*r*=0.315 *P*=0.026	*r*=0.327 *P*=0.039
Postoperative Day 1 (none/1 times/2 times)	*r*=0.462 *P*<0.0001	*r*=0.436 *P*=0.005
Postoperative Day 2 (none/1 times/2 times)	*r*=0.557 *P*<0.0001	*r*=0.229 *P*=0.156
Age (years)	*r*=0.318 *P*=0.018	*r*=0.329 *P*=0.038

NLR=Neutrophil-to-lymphocyte ratio

both groups, additional analgesic requirement was found to be positively correlated with preoperative NLR.

Discussion

NLR is calculated using the neutrophil and lymphocyte counts in whole blood tests, and nowadays popularity is increasing day by day. NLR has also been used as a marker for disease activity in various autoimmune conditions and has been shown to be a prognostic factor in malignancies.[6-8] The effect of general or regional anesthesia on pro-inflammatory and anti-inflammatory cytokines, where the applied regional anesthesia techniques suppressed the neuroendocrine stress response due to sympathetic blockade, has been demonstrated in previous studies.[9] However, there are not enough data on the effect of the selected postoperative analgesia technique, albeit only a small number of studies exist on the NLR effect of the anesthetic selection in the literature. In a study comparing sevoflurane with inhalation anesthesia and total intravenous anesthesia (TIVA), the NLR was lower in the TIVA group after 2 h of surgery.[10] In another study, patients undergoing a cesarean section with either general anesthesia or spinal anesthesia were compared, and the postoperative NLR was higher in the general anesthesia group.[11] Similarly, in this study, NLR was found to have a 9.23-fold increase in the group that received IV analgesia. The rate of increase was significantly higher in the group receiving IV analgesia than in the group treated with TEA.

One of the interesting results of our study was that the preoperative NLR was significantly higher in Group 1 patients. This can be explained by the fact that the patients in Group 1 are older, and the number of patients who undergo thoracotomy due to a lung mass is greater. Furthermore, studies have reported that NLR, an inflammatory marker, is associated with clinicopathologic features of many tumoral diseases and plays a significant role in the prognosis of many tumor patients, including those with lung tumors.[12] The high incidence of these patients in Group 1 was entirely random because we did determine our patients according to preoperative NLR. However, this has had a favorable outcome for patients. Studies have shown that long-term morbidity and mortality rates are higher in patients with high NLRs.[13] In our study, although the preoperative NLRs were higher in the epidural analgesia group, the NLR increase rates after 24 h were significantly lower than those in the IV analgesia patients. From this study, it does appear that administration of TEA decreases the NLR in the immediate postoperative period. The underlying mechanism should be investigated.

We think that there may be another reason for selecting regional analgesia methods in patients with high preoperative NLRs.

TEA is now accepted as the gold standard for post-thoracotomy pain because it provides better analgesia than the other methods. Epidural analgesia, which leads to positive effects such as improving pulmonary functions, thromboembolic complications, and reducing myocardial oxygen demand, is a preferred method in the treatment of post-thoracotomy pain. The multimodal analgesic approach, using more than one analgesic technique or drug, enhances efficacy in the

control of pain after thoracic surgery compared with a single analgesic approach.[1] Therefore, IV is often used for this purpose with opioids. The relationship between NLR and postoperative pain in patients undergoing orthognathic surgery has been investigated, and researchers have reported that postoperative analgesic requirements are higher in patients with a preoperative NLR ≥2.[14] In another study, however, the relationship between NLR and analgesic consumption after laparoscopic cholecystectomy was reported to be higher in postoperative analgesia consumption in patients with a low NLR.[15] In this study, we also found that the additional postoperative analgesic requirement was higher in the group of IV analgesia patients with lower preoperative NLRs. However, patients in the epidural analgesia group with a higher preoperative NLR and fewer additional analgesic requirements can be explained by the availability of effective analgesia in this TEA patient group. One missing aspect in this investigation is pain scoring to assess postoperative pain, which was not possible because the study design was retrospective.

Although there is no correlation between NLR and the incidence of atrial fibrillation in thoracic surgery,[16] it is known that there is a strong association between atrial fibrillation and NLR, especially in cardiac surgery.[17] Thus, although the rate of atrial fibrillation is beyond the scope of our study, the fact that NLR rate increase is lower in patients who undergo epidural analgesia may reduce the likelihood of atrial fibrillation. We think that new studies could shed some light on this issue.

Conclusion

In conclusion, this study has demonstrated that the type of analgesia plays a role in postoperative NLR change and that TEA is a more appropriate method for pain control in thoracotomy patients. We also think that because the preoperative NLR values are simple to calculate, clinical application should be recorded, and effective regional analgesia methods should be preferred in patients with a high NLR rate.

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Conflicts of interest

There are no conflicts of interest.

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