Original Article

Neutrophil Lymphocyte Ratio Predicts Postoperative Pain after Orthognathic Surgery

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Abstract

Background and Aim: Postoperative pain is well known and usually disturbing complication of surgery. Inflammation plays an important role in the development and progression of postoperative pain. We aimed to investigate possible relationship between preoperatively measured neutrophil-lymphocyte ratio (NLR) – as an inflammation marker – and postoperative analgesic demand in patients underwent orthognathic surgery. **Materials and Methods:** We retrospectively investigated medical and anesthesia records of 177 patients underwent orthognathic surgery. Demographical data, preoperative NLR, type of surgery, modified Mallampati score, difficulty degree of intubation, duration of surgery, and postoperative analgesic (tenoxicam – as the first drug of choice, paracetamol, tramadol, or pethidine) usage were recorded. A cutoff value of NLR ≥2 was determined for inflammation threshold. Two groups (Group 1 NLR ≥2, Group 2 NLR <2) were compared for analgesic doses, numbers of patients needed analgesic treatment, and other parameters. **Results:** Mean administered tenoxicam dose was significantly higher in Group 1 than in Group 2 ($P < 0.0001$). Further, ratio of patients treated with tenoxicam in Group 1 was significantly higher than that in Group 2 ($\chi^2 = 4.779$, $P = 0.029$). **Conclusions:** Preoperatively measured NLR may help to predict postoperative analgesic demand in patients undergoing orthognathic surgery, and thus sufficient postoperative pain control can be achieved with various preventive treatments taken at the perioperative period such as preemptive analgesia, local anesthetic administration at the end of surgery, or early administration of analgesics.

Keywords: *Neutrophil-lymphocyte ratio, orthognathic, postoperative pain, tenoxicam*

Date of Acceptance:
21-Mar-2016

Introduction

Postoperative pain is one of the most uncomfortable situations related with surgery, and inadequate pain control may lead significantly increased morbidity and/or mortality. On the other hand, adequate management of postoperative pain results increased patient comfort and decreased mobilization time, systemic complications, and recovery period without disturbing memories related with surgery.[1] Inflammation triggered by surgical trauma secondary to incision, dissection, suturing, nerve stretching, or nerve compression takes part in mechanism of postoperative pain. Hyperalgesia and allodynia caused by released local inflammatory mediators are important factors for patients' pain perceptions.[2]

Neutrophil-lymphocyte ratio (NLR) is relatively new recognized inflammation marker and significant relationship between NLR and outcomes and/or prognosis of many clinical situations including different types of cancers (colorectal, gastric, pancreatic, esophageal, lung, etc.), systemic diseases (hypertension, type 2 diabetes mellitus),

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/1119-3077.181399

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How to cite this article: Turgut HC, Alkan M, Ataç MS, Altundağ SK, Bozkaya S, Şimşek B, *et al.* Neutrophil lymphocyte ratio predicts postoperative pain after orthognathic surgery. Niger J Clin Pract 2017;20:1242-5.

heart disease, inflammatory diseases (systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, etc.), and several others (cystic fibrosis, peripheral vertigo, etc.) have been shown.[3-15]

In this study, we aimed to investigate possible relationship between preoperative NLR and postoperative pain (which was evaluated by analgesic demand at postoperative period) in patients underwent different orthognathic surgical procedures.

Materials and Methods

This study was approved by the Ethics Committee of Gazi University Hospital. We performed a retrospective analysis of clinical and anesthesia reports of 177 patients – of whom, 37 patients' data were excluded due to lacking surgical data and final number of patients included was 140 who underwent several different types of orthognathic surgery procedures (bilateral sagittal split ramus osteotomy, Le Fort I, Le Fort II, maxilla-facial fracture fixation). Age, sex, type of surgery, preoperative NLR, the modified Mallampati score,[16] difficulty degree of intubation, duration of surgery, and amount of administered analgesic drugs were recorded. While performing the modified Mallampati score the view of intraorally structures is graded as follows to predict risk of difficult laryngoscopy/intubation: Class I, soft palate, fauces, uvula, and pillars visible; Class II, soft palate, fauces, and uvula visible; Class III, soft palate and base of the uvula visible; Class IV, soft palate not visible. The patients are placed in a sitting position with the head in a neutral potion, and the assessment is performed without phonation. Mallampati score of III or IV is considered a risk factor for difficult laryngoscopy/intubation.[16] Various analgesic drugs were used for treatment of postoperative pain; tenoxicam intravenous [iv] was the first choice of analgesic. Paracetamol iv, tramadol iv, and/or pethidine iv was administered in addition to tenoxicam when needed. A threshold of ≥2 for preoperative NLR was determined high and as the indicator of an inflammatory status according to various previous studies[11,12,17,18] which showed significant differences in investigated clinical outcomes (survival, disease activity, etc.) between patients with NLR ≥2 and <2 and subsequently two groups were constituted.

Statistical analysis

The statistical analyses were performed using SPSS software for windows version 20.0 (IBM Corp, Armonk, NY, USA) and $P < 0.05$ was considered statistically significant. Kolmogorov–Smirnov test was performed for the measurable parameters to determine whether the range is normal. Parametric values were evaluated with Student's *t*-test. Mallampati score, difficulty degree of intubation, and number of patients requiring analgesics were compared using Chi-square and Fisher's exact tests.

Results

Medical records of 140 patients (M = 68, F = 72) were evaluated. Mean age of patients in two study groups was similar (32 vs. 29.9 years, $P = 0.367$). There was no difference between demographical data of patients ($P > 0.05$) [Table 1]. There were no statistically significant differences between groups in terms of surgery type ($P > 0.05$). Modified Mallampati scores and difficulty degree of intubation were similar between groups ($P = 0.185$ and $P = 0.392$, respectively) [Table 1]. There was only one patient in each group with a modified Mallampati score of 4, and difficult intubation was occurred in only one patient in Group 2 and was intubated successfully at the 3rd attempt. A cutoff value of ≥2 was determined for NLR in accordance with previous studies.[11,12,19,20] In Group 1, preoperative NLR was ≥2 while in Group 2, NLR was <2. Mean amount of tenoxicam iv administered in Group 1 was significantly higher than those in Group 2 (32.00 ± 13.99 vs. 24.33 ± 8.31 mg) and difference was statistically significant ($P < 0.0001$) [Table 2].

In Group 1, ratio of patients treated with tenoxicam iv was 87.7% while 72.3% in Group 2, and difference was statistically significant ($\chi^2 = 4.779$, $P = 0.029$) [Table 2]. In addition, mean administered tenoxicam dose in

Table 1: Demographical data of patients (mean±standard deviation (minimum-maximum), *n* (%))

	Group 1 (*n*=57)	Group 2 (*n*=83)	*P*
Age	32.00±13.65	29.90±13.34	0.367
Neutrophil lymphocyte ratio	3.28±2.72	1.42±0.334*	<0.0001
Duration of surgery	203.85±110.73	215.90±110.68	0.528
Mallampati score (1/2/3/4)	55 (96.5)/1 (1.8)/ 0 (0)/1 (1.8)	75 (90.4)/3 (3.6)/ 4 (4.8)/1 (1.2)	0.185
Difficulty degree of intubation (1/2/3/4)	55 (96.5)/0 (0)/ 2 (3.5)/0 (0)	81 (97.6)/0 (0)/ (1.2)/1 (1.2)	0.392

*P<0.05 (compared to Group 1). SD=Standard deviation

Table 2: Data regarding analgesic treatment (mean±standard deviation (minimum-maximum), *n* (%))

	Group 1 (*n*=57)	Group 2 (*n*=83)	*P*
Tenoxicam (mg)	32.00±13.99	24.33±8.31*	<0.0001
Numbers of patients treated with tenoxicam (*n*)	50 (87.7)	60 (72.3)*	χ^2=4.779 0.029
Tramadol (*n*)	12 (21.1)	13 (15.7)	0.413
Pethidine (*n*)	3 (5.3)	3 (3.6)	0.687
Paracetamol (*n*)	14 (24.6)	17 (20.5)	0.568

*P<0.05 (compared to Group 1). SD=Standard deviation

Group 1 was significantly higher than that in Group 2 (32.00 ± 13.99 vs. 24.33 ± 8.31, respectively, $P < 0.0001$) [Table 2]. In Group 1, 12 patients (21.1%) were treated with tramadol iv while in Group 2, 13 patients (15.7%) were treated with same analgesic drug ($P = 0.413$). In Group 1, 14 patients (24.6%) received paracetamol iv while 17 patients (20.5%) in Group 2 received paracetamol iv ($P = 0.568$). Moreover, number of patients received pethidine was similar between groups (3 vs. 3 patients, $P = 0.687$).

Discussion

Our study pointed out that preoperative NLR is a useful tool for predicting postoperative analgesic demand and –indirectly – pain levels of patient underwent orthognathic surgery. To our knowledge, this is the first study showing the relationship between preoperative NLR and postoperative analgesic demand.

It is well known that systemic inflammation results in lymphopenia and neutrophilia.[11] NLR is a newly recognized marker of subclinical inflammation and is thought to indicate the equilibrium between innate (neutrophils) and adaptive (lymphocytes) immune responses. NLR has been used in many clinical investigations with or without other inflammatory markers to determine inflammation and/or disease prediction, prognosis, and outcomes in many different clinical entities.[3-15] The predictive role of NLR, as an inflammation marker, in several diseases such as coronary artery disease, cancers, and inflammatory diseases suggests that NLR can be a useful predictive tool for postoperative pain resulted from inflammatory pathways secondary to surgical trauma and/or surgery-related direct nerve trauma. NLR can be easily calculated and cheap because it is derived from complete blood count that routinely performed during preoperative period without any additional cost.

The only study in literature investigating possible relationship between preoperative NLR and postoperative pain enrolled sixty patients, who underwent laparoscopic cholecystectomy under general anesthesia.[19] The total analgesic requirements during the first 48 h at postoperative period were the primary endpoint (unitary dosage [UD]), and also authors evaluated association between preoperative NLR and total analgesic requirement (UD). The authors identified the UD as the number of times, the patient requested an analgesic and each time, the patient requested an analgesic corresponds to a UD. The total UD during the late postoperative 48 h represents the analgesic requirement of patient. The main result of this study summarized that preoperative pain-related attitudes measured with situational pain scale were associated with the postoperative analgesic requirements (UD) after a cholecystectomy. In addition, 80% of this effect was mediated by emotional status of the patient and NLR. Further, lower NLR was found in correlation with higher analgesic requirements represented by UD. In contrast to this study, we found positive correlation between higher preoperative NLR and postoperative analgesic consumption (accepted as an indicator of postoperative pain). We suggest that different methods used for evaluating postoperative pain and analgesic treatment, total amount of administered tenoxicam versus number of times the patient requested an analgesic, may lead the contrary results of two studies.

There are no established certain cutoff values for NLR in; indeed, important differences between races even for same clinical conditions have been reported.[20] In our study, we used a cutoff value of NLR ≥2.0 to be significantly associated with an inflammatory condition which is consistent with prior findings by Jung *et al*.[17] and Hong *et al*.[18] who showed that NLR >2 predicts poor outcomes in two different cancer types. In addition to cancer studies, an NLR value >2 was identified as significant cutoff value in different clinical studies investigating relationship between NLR and inflammatory diseases such as systemic lupus erythematosus (NLR = 2.065)[12] and rheumatoid arthritis (NLR = 2.12 ± 0.83 in the patient group).[11]

Previously described predictors of postoperative pain include preoperative pain, type of surgery (orthopedic, joint, abdominal, thoracic surgery), obesity, young age, and preoperatively anxiety about anesthesia and surgery.[21] Beside these factors, our study results indicate that NLR may help estimating postoperative pain level after orthognathic surgery. In this way, using preoperative NLR values anesthetist can make decision about amount, timing, and type of analgesic usage.

Limitations

This study is a retrospectively designed study; therefore, lacking interventions provide more strong correlations. Despite retrospective design of study, we can say that we still found meaningful relation between preoperative studied NLR and postoperative analgesic demand.

Conclusion and Recommendations

Preoperative NLR may be a potential predictor of pain levels after orthognathic surgery and so more reliable and sufficient pain control through choices such as preemptive analgesia, early administration of analgesics, or local anesthesia can be managed in accordance with preoperative NLR values. Future prospective studies are warranted to validate our findings and determine cutoff values for NLR in different populations and clinical situations.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Ramsay MA. Acute postoperative pain management. Proc (Bayl Univ Med Cent) 2000;13:244-7.
2. Kelly DJ, Ahmad M, Brull SJ. Preemptive analgesia I: Physiological pathways and pharmacological modalities. Can J Anaesth 2001;48:1000-10.
3. Ying HQ, Deng QW, He BS, Pan YQ, Wang F, Sun HL, *et al.* The prognostic value of preoperative NLR, d-NLR, PLR and LMR for predicting clinical outcome in surgical colorectal cancer patients. Med Oncol 2014;31:305.
4. Shimada H, Takiguchi N, Kainuma O, Soda H, Ikeda A, Cho A, *et al.* High preoperative neutrophil-lymphocyte ratio predicts poor survival in patients with gastric cancer. Gastric Cancer 2010;13:170-6.
5. Stotz M, Gerger A, Eisner F, Szkandera J, Loibner H, Ress AL, *et al.* Increased neutrophil-lymphocyte ratio is a poor prognostic factor in patients with primary operable and inoperable pancreatic cancer. Br J Cancer 2013;109:416-21.
6. Sharaiha RZ, Halazun KJ, Mirza F, Port JL, Lee PC, Neugut AI, *et al.* Elevated preoperative neutrophil: Lymphocyte ratio as a predictor of postoperative disease recurrence in esophageal cancer. Ann Surg Oncol 2011;18:3362-9.
7. Lee Y, Kim SH, Han JY, Kim HT, Yun T, Lee JS. Early neutrophil-to-lymphocyte ratio reduction as a surrogate marker of prognosis in never smokers with advanced lung adenocarcinoma receiving gefitinib or standard chemotherapy as first-line therapy. J Cancer Res Clin Oncol 2012;138:2009-16.
8. Liu X, Zhang Q, Wu H, Du H, Liu L, Shi H, *et al.* Blood neutrophil to lymphocyte ratio as a predictor of hypertension. Am J Hypertens 2015;28:1339-46.
9. Guo X, Zhang S, Zhang Q, Liu L, Wu H, Du H, *et al.* Neutrophil: Lymphocyte ratio is positively related to type 2 diabetes in a large-scale adult population: A tianjin chronic low-grade systemic inflammation and health cohort study. Eur J Endocrinol 2015;173:217-25.
10. Shah N, Parikh V, Patel N, Patel N, Badheka A, Deshmukh A, *et al.* Neutrophil lymphocyte ratio significantly improves the Framingham risk score in prediction of coronary heart disease mortality: Insights from the National Health and Nutrition Examination Survey-III. Int J Cardiol 2014;171:390-7.
11. Qin B, Ma N, Tang Q, Wei T, Yang M, Fu H, *et al*. Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. Mod Rheumatol 2016;1-5. [Epub ahead of print].
12. Uslu AU, Küçük A, Sahin A, Ugan Y, Yilmaz R, Güngör T, *et al.* Two new inflammatory markers associated with disease activity score-28 in patients with rheumatoid arthritis: Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio. Int J Rheum Dis 2015;18:731-5.
13. Acarturk G, Acay A, Demir K, Ulu MS, Ahsen A, Yuksel S. Neutrophil-to-lymphocyte ratio in inflammatory bowel disease-as a new predictor of disease severity. Bratisl Lek Listy 2015;116:213-7.
14. O'Brien CE, Price ET. The blood neutrophil to lymphocyte ratio correlates with clinical status in children with cystic fibrosis: A retrospective study. PLoS One 2013;8:e77420.
15. Ozbay I, Kahraman C, Balikci HH, Kucur C, Kahraman NK, Ozkaya DP, *et al.* Neutrophil-to-lymphocyte ratio in patients with peripheral vertigo: A prospective controlled clinical study. Am J Otolaryngol 2014;35:699-702.
16. Samsoon GL, Young JR. Difficult tracheal intubation: A retrospective study. Anaesthesia 1987;42:487-90.
17. Jung MR, Park YK, Jeong O, Seon JW, Ryu SY, Kim DY, *et al.* Elevated preoperative neutrophil to lymphocyte ratio predicts poor survival following resection in late stage gastric cancer. J Surg Oncol 2011;104:504-10.
18. Hong J, Mao Y, Chen X, Zhu L, He J, Chen W, *et al.* Elevated preoperative neutrophil-to-lymphocyte ratio predicts poor disease-free survival in Chinese women with breast cancer. Tumour Biol 2015;. [Epub ahead of print].
19. Daoudia M, Decruynaere C, Le Polain de Waroux B, Thonnard JL, Plaghki L, Forget P. Biological inflammatory markers mediate the effect of preoperative pain-related behaviours on postoperative analgesics requirements. BMC Anesthesiol 2015;15:183.
20. Azab B, Camacho-Rivera M, Taioli E. Average values and racial differences of neutrophil lymphocyte ratio among a nationally representative sample of United States subjects. PLoS One 2014;9:e112361.
21. Corke P. Postoperative pain management. Aust Prescr 2013;36:202-5.