To cite this article: Ülger G, Baldemir R, Zengin M, Sazak H, Alagöz A. Demographic, Clinical, and Laboratory Parameters in Predicting Postoperative Nausea/Vomiting in Patients with Thoracic Epidural Analgesia in Thoracic Surgery. Turk J Clin Lab 2022; 1: 22-28.

Original Article

# Demographic, Clinical, and Laboratory Parameters in Predicting Postoperative Nausea/Vomiting in Patients with Thoracic Epidural Analgesia in Thoracic Surgery

## *Göğüs Cerrahisi Ameliyatı Geçiren Torakal Epidural Kateter Takılan Hastalarda Postoperatif Bulantı/Kusmayı Öngörmedeki Parametreler*

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## Abstract

**Aim:** In thoracic surgery, many factors; such as the long duration of surgery and the use of volatile anesthetics may increase the frequency of postoperative nausea/ vomiting (PONV). Recent studies suggest that inflammatory markers such as neutrophil lymphocytes ratio (NLR) can predict PONV. This study aims to postoperatively examine the role of demographic, laboratory, and clinical data in predicting PONV in patients who underwent thoracotomy and received thoracic epidural analgesia (TEA).

**Material and Methods:** Data were collected for patients who underwent elective thoracic surgery and were administered TEA between March 2017 and December 2020. Patients' demographic data, laboratory parameters, and clinical characteristics; such as American Association of Anesthesiologists (ASA) physical score, erythrocyte distribution width (RDW), NLR, postoperative visual analog scale (VAS), were scanned. All patients who developed PONV were included in Group 1. Hospital records were used to select Group 2 patients who did not develop PONV.

**Results:** The incidence of PONV was determined as 14.77%. There was a statistically significant difference between the groups in terms of ASA and 24-hour VAS scores ($p < 0.05$). Patients with PONV had statistically significantly higher 24-hour VAS scores ($p < 0.05$). PONV was statistically significantly higher in patients with ASA III compared to other ASA groups ($p < 0.05$). Multivariate analysis suggests that ASA, RDW, and 24-hour VAS are significant in predicting PONV. Lower RDW, higher ASA, and 24-hour VAS increase the risk of PONV.

**Conclusion:** Demographic data, laboratory parameters, and clinical characteristics were evaluated concerning their correlation with PONV in this study. It was observed that the frequency of PONV might increase in patients with low RDW levels. In addition, higher VAS values and ASA physical scores were also found to increase the risk of PONV in patients who underwent thoracotomy and administered TEA

**Keywords:** Postoperative nausea/vomiting; PONV; thoracic epidural analgesia; thoracic surgery.

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Received: 05.11.2021 accepted: 21.12.2021
Doi: 10.18663/tjcl.1019702

TJCL Volume 13 Number 1 p: 22-28


## Öz

**Amaç:** Ameliyat süresinin uzun olması ve volatil anesteziklerin kullanılması gibi birçok faktör göğüs cerrahisinde postoperatif bulantı/kusma (PONV) sıklığını artırabilir. Son çalışmalar, nötrofil lenfosit oranı (NLR) gibi inflamatuar parametrelerin PONV'yi öngörebileceğini düşündürmektedir. Bu çalışmanın amacı, torakotomi ameliyatı olan ve torasik epidural analjezi (TEA) uygulanan hastalarda postoperatif demografik, laboratuvar ve klinik verilerin PONV'yi öngörmedeki rolünü incelemektir.

**Gereç ve Yöntemler:** Mart 2017 - Aralık 2020 tarihleri arasında elektif göğüs cerrahisi geçiren ve TEA uygulanan hastaların verileri taranmıştır. Hastaların demografik verileri, laboratuvar parametreleri, Amerikan Anestezistler Birliği (ASA) fiziksel skorları, eritrosit dağılım genişliği (RDW), NLR, postoperatif vizuel analog skala (VAS) gibi klinik özellikleri incelenmiştir. PONV gelişen tüm hastalar Grup 1'e dâhil edilmiştir. PONV gelişmeyen Grup 2 hastalarını seçmek için hastane kayıtları kullanılmıştır.

**Bulgular:** PONV insidansı %14.77 olarak belirlendi. ASA ve 24 saatlik VAS skorları açısından gruplar arasında istatistiksel olarak anlamlı fark vardı ($p < 0.05$). PONV'li hastalarda istatistiksel olarak anlamlı şekilde daha yüksek 24 saatlik VAS skorları vardı ($p < 0.05$). ASA III olan hastalarda PONV diğer ASA gruplarına göre istatistiksel olarak anlamlı şekilde daha fazla görüldü ($p < 0.05$). Çok değişkenli analiz; ASA, RDW ve 24 saatlik VAS'ın PONV'yi öngörmede önemli olduğunu göstermektedir. Daha düşük RDW, daha yüksek ASA ve 24 saatlik VAS, PONV riskini artırır.

**Sonuç:** Bu çalışmada demografik veriler, laboratuvar parametreleri ve klinik özellikler PONV ile korelasyonları açısından değerlendirildi. RDW düzeyi düşük olan hastalarda PONV sıklığının artabileceği gözlendi. Ayrıca torakotomi yapılan ve TEA uygulanan hastalarda yüksek VAS değerleri ve ASA fiziksel skorlarının da PONV riskini artırdığı bulundu.


**Anahtar Kelimeler:** Postoperatif bulantı/kusma; PONV; torasik epidural analjezi; torasik cerrahi.

## Introduction

The prevalence of postoperative nausea/vomiting (PONV) is found to be in a wide range of 34%-80% [1]. PONV is defined as retching, nausea, or vomiting that develops in the first 24 hours after surgery [2,3]. In patients undergoing thoracic surgery, the long duration of surgery and the use of volatile anesthetics may increase the frequency of PONV. PONV negatively affects patient comfort and can cause many problems such as dehydration, electrolyte imbalance, venous hypertension, esophageal rupture, separation of surgical suture lines, and life-threatening airway obstruction due to aspiration [4]. In the literature, many factors such as demographic characteristics of patients, anesthetic methods applied, opioid usage, duration of surgery, and type of surgery determine the incidence of PONV [5]. Inflammation is counted among several factors that increase the risk of nausea/vomiting [2]. Therefore, a relation can be detected between a parameter that is an indicator of inflammation and nausea/vomiting. Parameters such as Neutrophil/Lymphocyte Ratio (NLR) and Erythrocyte Distribution Width (RDW), which are routinely checked in all patients before surgery and can be calculated by complete blood count, can be evaluated as indicators of systemic inflammation. Therefore, a correlation between these parameters and PONV can be investigated. Recent studies are showing that inflammatory markers such as NLR can predict PONV [2, 3]. However, there were no studies on patients at risk for PONV and the incidence of PONV in thoracic surgery. Therefore, evaluation of patients at risk for PONV in thoracic surgery operations, determination of the frequency of PONV in this patient group, and preoperative prediction of patients who may develop PONV may provide valuable contributions to the management of postoperative patient treatment.

This study aims to investigate the role of demographic, laboratory parameters, and clinical characteristics in predicting PONV in patients who underwent thoracotomy and received thoracic epidural analgesia (TEA).

## Material and Method

After the approval of the Local Ethical Committee (approval decision ID Number: 730, Date: 17.06.2021), the anesthesia and postoperative pain forms of patients who underwent elective thoracic surgery and were administered TEA between March 2017 and December 2020 were retrospectively evaluated.

Patients who had undergone thoracotomy with the same type of anesthesia (volatile anesthetic) and received TEA were included in our study. Patients who are between the ages of 18-80 years, are in the American Association of Anesthesiologists (ASA) I-II-III physical status (PS), have a body mass index (BMI) between 18.5 and 35 kg/m2, and were received TEA were included in our study.

Patients with the following criteria were excluded: Under

the age of 18 and over the age of 80 years, ASA PS IV and above, a BMI below 18.5 and above 35 kg/m2, severe systemic inflammatory disease, gastrointestinal disease, missing data, receiving intraoperative blood product transfusion, usage of constant anti-inflammatory drugs, steroids and antiemetic drugs. Moreover, patients undergoing emergency surgery and receiving a method other than volatile anesthesia and TEA were not included.

Patients' age, height, body weight, BMI, gender, diagnosis, ASA PS, preoperative neutrophils, lymphocytes, monocytes, platelet values, RDW, NLR, surgical procedure, duration of surgery, perioperative complications, postoperative Visual Analog Scale (VAS) score, whether there was a complaint of nausea/vomiting in the first 24 hours after surgery, perioperative antiemetic drug usage and doses were determined. NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

The patients were divided into two groups. All patients who underwent thoracotomy received TEA, and developed PONV; were included in Group 1. Hospital records were used to select Group 2 patients who underwent thoracotomy, received TEA, and did not develop PONV.

Standard anesthesia management and perioperative analgesia protocol, which is routinely used in the clinic, was applied to patients who underwent thoracotomy and received TEA. As a volatile anesthetic, 2-3% sevoflurane was administered in an oxygen/air mixture. In addition, intraoperative analgesia was provided by epidural infusion. In the intraoperative period; for TEA, 67.5 ml of bupivacaine, 201.5 ml of saline, and 10 mg/1 ml of morphine were given with a 270 ml elastomeric infusion pump. Bupivacaine 0.125% was administered epidurally with an elastomeric pump at a rate of 4 ml/hr for 3 days postoperatively.

Right before the end of the surgery in all patients, 50 mg of dexketoprofen and 100 mg of tramadol were given to contribute to postoperative analgesia, and 10 mg of metoclopramide was administered to prevent PONV. Postoperative epidural analgesia treatment with an elastomeric infusion pump was continued in the postoperative intensive care unit. Besides, dexketoprofen 50 mg in every 12 hours and paracetamol 1 g in every 6 hours were administered as routine intravenous analgesia protocol. Tramadol 50 mg was administered intravenously as "rescue analgesia" in the patients with VAS 4 and above.

In the postoperative follow-up; complications if any, postoperative VAS, presence of PONV in the first 24 hours, whether antiemetic drugs were given after PONV, and the doses of antiemetic drugs were determined from the postoperative analgesia follow-up forms.

## Statistical Analysis

Data analyses were performed by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). Whether the distribution of continuous variables were normal or not was determined by the Kolmogorov-Smirnov test. Levene's test was used for the evaluation of homogeneity of variances. Unless specified otherwise, continuous data were described as mean ± standard deviation for normal distributions, and median (interquartile range) for skewed distributions. Categorical data were described as the number of cases (%).

Statistical analysis differences in normally distributed variables between two independent groups were compared by Student's t-test. The Mann-Whitney U tests were applied for comparisons of the not normally distributed data. Categorical variables were compared using Pearson's Chi-Square test or Fisher's Exact test.

First, one variable binary logistic regression analysis was used with risk factors that are thought to be related to nausea/vomiting. Risk factors that have a p-value < 0.25 at one variable logistic regression were included in the multinomial logistic regression model as independent variables. Whether every independent variable was significant on the model was analyzed with Wald statistic. Nagelkerke's R2 was used to evaluate that an independent variable explained how much of the dependent variable. Besides, it was evaluated model adaptation of estimates with Hosmer and Lemosow model adaptation test. ROC curve analysis was used to determine the cut-off points. It was accepted p-value < 0.05 as a significant level on all statistical analyses. It was accepted p-value > 0.05 and p-value < 0.10 as marginally significant level on all statistical analyses.

## Results

A total of 389 patients who underwent elective thoracotomy and received TEA between March 2017 and December 2020 were retrospectively analyzed. 10 of these patients were excluded because their thoracic epidural catheters failed within postoperative 24 hours. 14 patients were excluded because they did not meet the inclusion criteria, and 13 patients were excluded because their data were missing. Data from a total of 352 patients were analyzed (Figure 1).

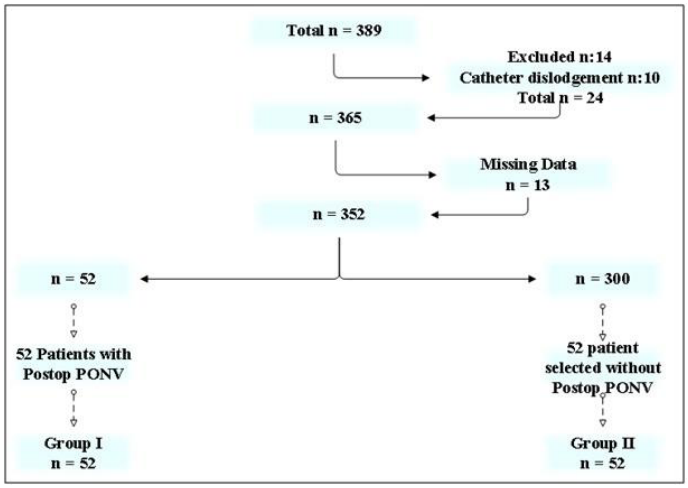


**Figure 1** Flow chart of the patients

Demographic data, preoperative laboratory data, pain scores, and postoperative complications of the patients in PONV and control groups are shown in Table 1.

When the demographic data and clinical characteristics of the patients were evaluated, there was a statistically significant difference between the groups in terms of ASA PS and 24-hour VAS scores average. Patients with PONV had a statistically significantly higher 24-hour VAS average and ASA III PS rate than patients without PONV ($p < 0.05$) (Table 1).

One variable binary logistic regression analysis was applied to determine whether preoperative laboratory parameters and other variables were effective in predicting PONV. According to one variable binary logistic regression analysis variables with a p-value below 0.25 were included in the multivariate analysis. According to the results of multivariate analysis; it has been understood that ASA, RDW, and 24-hour VAS average play an active role in predicting PONV. Lower RDW, higher ASA PS, and 24-hour VAS average increase the risk of PONV (Table 2).

According to ROC analysis, RDW (AUC: 0.601, $p = 0.075$) and NLR (AUC: 0.536, $p = 0.533$) variables were not meaningful to predict PONV. Therefore, cut-off value could not be determined.

**Table 1 –** Patient's demographic data, clinical characteristics, preoperative laboratory data, pain scores, and postoperative complications

| | | Group 1 (n=52) | Group 2 (n=52) | Total (n=104) | p |
|---|---|---|---|---|---|
| Age (year) | | 49.62 ± 14.44 | 50.19 ± 14.13 | 49.90 ± 14.22 | 0.837 |
| Gender | Female | 7 (13.5%) | 7 (13.5%) | 14 (13.5%) | 0.999 |
| | Male | 45 (86.5%) | 45 (86.5%) | 90 (86.5%) | |
| BMI (kg/m2) | | 25.52 ± 4.10 | 25.58 ± 3.70 | 25.55 ± 3.89 | 0.94 |
| Operation | Segmentectomy Lobectomy | 42 (80.8%) | 37 (71.2%) | 79 (76.0%) | 0.386 |
| | Pneumonectomy | 7 (13.5%) | 8 (15.4%) | 15 (14.4%) | |
| | Decortication | 3 (5.8%) | 4 (7.7%) | 7 (6.7%) | |
| | Cystotomy with Capitonnage | - | 3 (5.8%) | 3 (2.9%) | |
| Duration of Operation (min) | | 235 (30) | 240 (37.5) | 237.5 (35) | 0.67 |
| ASA | 2 | 26 (50.0%) | 38 (73.1%) | 64 (61.5%) | 0.016 |
| | 3 | 26 (50.0%) | 14 (26.9%) | 40 (38.5%) | |
| Lymphocyte | | 1.97 ± 0.74 | 2.08 ± 0.86 | 2.02 ± 0.80 | 0.504 |
| Monocyte | | 0.49 (0.25) | 0.52 (0.27) | 0.50 (0.26) | 0.728 |
| Neutrophil | | 5.17 (3.61) | 5.01 (4.21) | 5.01 (3.93) | 0.823 |
| Thrombocytes | | 282.85 ± 87.54 | 282.56 ± 84.49 | 282.70 ± 85.61 | 0.986 |
| RDW | | 14.65 (2.15) | 15.15 (2.75) | 14.90 (2.35) | 0.075 |
| Neutrophil/Lymphocyte Ratio | | 2.77 (2.71) | 2.39 (2.26) | 2.53 (2.53) | 0.533 |
| 24 Hour VAS Scores | | 3 (1.2) | 2.7 (1) | 2.8 (1) | 0.02 |
| Headache | | 22 (42.3%) | - | 22 (21.2%) | <0.001 |
| Hypotension | | 10 (19.2%) | - | 10 (9.6%) | 0.001 |
| Rescue Analgesia | | 7 (13.7%) | 7 (13.5%) | 14 (13.6%) | 0.969 |

Normally distributed quantitative data were evaluated with (Mean) ± SD (Standard Deviation) and non-normally distributed quantitative data were evaluated with median (interquartile range) while qualitative data were evaluated with numbers (percentage). In the comparisons between groups, the Student t-test was used for normally distributed quantitative data consisting of 2 groups, Mann-Whitney U test was used for data not showing normal distribution, and Chi-Square Test or Fisher's Exact Test was used for qualitative data.
PONV: Postoperative nausea/vomiting, min: (minutes), ASA: American Society of Anesthesiologists, RDW: Erythrocyte Distribution Width, VAS: Visual Analog Scale, BMI: Body Mass Index

**Table 2 -** One variable and multivariable regression analysis

| | One Variable Logistic Regression | | | | Multivariable Logistic Regression | | | |
|---|---|---|---|---|---|---|---|---|
| | Wald | P | OR | 95% CI | Wald | p | OR | 95% GA |
| Age | 0.043 | 0.835 | 0.997 | (0.970-1.025) | | | | |
| Gender | 0.000 | 0.999 | 1.000 | (0.324-3.084) | | | | |
| BMI | 0.006 | 0.939 | 0.996 | (0.902-1.100) | | | | |
| ASA | 5.708 | 0.017 | 2.714 | (1.196-6.157) | 6.844 | 0.009 | 3.280 | (1.347-7.985) |
| Duration of Operation | 0.326 | 0.568 | 0.997 | (0.985-1.008) | | | | |
| Lymphocyte | 0.455 | 0.500 | 0.845 | (0.519-1.378) | | | | |
| Monocyte | 0.098 | 0.754 | 1.287 | (0.265-6.249) | | | | |
| Neutrophil | 0.002 | 0.967 | 1.003 | (0.881-1.141) | | | | |
| RDW | 4.873 | 0.027 | 0.780 | (0.626-0.973) | 5.132 | 0.023 | 0.760 | (0.600-0.964) |
| Thrombocytes | 0,000 | 0.986 | 1.000 | (0.996-1.005) | | | | |
| NLR | 0.103 | 0.749 | 0.981 | (0.875-1.101) | | | | |
| VAS Mean | 4.512 | 0.034 | 1.610 | (1.037-2.498) | 3.940 | 0.047 | 1.597 | (1.006-2.534) |
| Additional Analgesic | 0.681 | 0.409 | 2.083 | (0.365-11.905) | | | | |

WALD; Logistic regression test statistic, OR; Odds ratio, CI; confidence interval. Hosmer and Lemeshow p>0.05, ASA: American Society of Anesthesiologists, RDW: Erythrocyte Distribution Width, VAS: Visual Analog Scale, BMI: Body Mass Index, NLR: Neutrophil/Lymphocyte Ratio

## Discussion

According to the results of our study, the incidence of PONV was determined as 14.77% in patients who underwent thoracotomy and received TEA. It was observed that RDW, ASA PS, and 24-hour VAS average could be effective in predicting PONV.

PONV prolongs the recovery period of the patient due to the problems it creates in the postoperative period, increases the duration of the patient's hospital stay, and thus the treatment costs [6, 7]. A history of motion sickness or PONV, smoking habit, use of volatile anesthetics or nitrous oxide, intraoperative or postoperative opioid use, long operation duration, and type of surgery are known to increase the risk of PONV [8]. In addition, inflammation increases the risk of PONV [2]. There are studies indicating that NLR is higher in patients with nausea/vomiting and that some hemogram parameters such as NLR, RDW, and thrombocyte measured preoperatively may be effective in predicting PONV [2, 3, 9, 10, 11]. Patients undergoing thoracic surgery may be at high risk for PONV due to the long operation time, the frequent use of volatile anesthetics and opioids, and the application of TEA due to severe postoperative pain. In our study, patients who underwent thoracotomy and were administered TEA for postoperative analgesia were examined by standardizing the anesthetic method, type of surgery, and postoperative analgesic method.

It has been stated that preoperative NLR and PONV may be related in studies on non-thoracic surgery patients. However, in our study, contrary to the literature results, it was observed that preoperative NLR was not an effective parameter in predicting PONV in patients who underwent thoracotomy and TEA.

On the other hand, we found a correlation between RDW and PONV. RDW expresses variations in erythrocyte volume, also known as anisocytosis, and although its mechanism is not fully understood, its elevation may indicate increased inflammation and oxidative stress [12]. RDW is an inflammatory marker and is evaluated as a prognostic indicator in many diseases [13-16]. In the literature; the relationship between RDW and PONV was evaluated in patients with a diagnosis of hyperemesis gravidarum. In these studies, when the control group and those with a diagnosis of hyperemesis gravidarum were evaluated, it was reported that RDW was not statistically different between the groups [17-19]. In a different study, it was reported that RDW was higher in patients with a diagnosis of hyperemesis gravidarum [20]. In our study, the RDW value was found to be lower in the group with PONV compared to the control group. This result was accepted as borderline significant. However, according to one variable and multivariate logistic regression analysis, a decrease in RDW increases the risk of PONV. The difference in the results obtained in pregnant women compared to our study may be attributed to the change in physiology in pregnant women and the difference in hormonal levels according to the gestational week. Therefore, studies that will investigate the relationship between RDW and PONV in non-pregnant patients are needed.

Another important result of our study is that the risk of PONV is high in patients with higher VAS values. This shows

the importance of postoperative pain control and PONV can be affected by many factors. There are limited studies in the literature on the relationship between PONV and postoperative pain. In a study, it was reported that gabapentin, which is used in the treatment of neuropathic pain, reduced PONV [21]. However, although the reduction mechanism was not fully revealed in the study, it was stated that gabapentin reduced morphine consumption. The decrease in PONV can be attributed to the decrease in morphine consumption. Similar to our study, a study reported that there was a correlation between postoperative pain and PONV [22]. However, a correlation was found between the need for additional analgesics and PONV [22]. This can be attributed to the increase in analgesic use. In our study, patients were administered standard epidural morphine infusion and tramadol was given to patients when they needed additional analgesics. Although it is thought that tramadol may cause nausea/vomiting, there is no statistically significant difference between the group with PONV and the control group in terms of tramadol use in our study.

There are studies reporting that ASA PS is associated with PONV. Low ASA PS has been reported to be one of the main risk factors for PONV [23, 24]. Another study stated that there was no significant relationship between ASA PS and PONV formation [25]. In our study, unlike these results, a positive correlation was observed between higher ASA PS and PONV. The results of the studies have also shown that it may not be possible to say that there is a clear relationship between ASA PS and PONV. Large-series randomized studies may clarify this issue.

One of the main components of enhanced recovery after surgery (ERAS) protocols, which has also been accepted in thoracic surgery, is the prevention of PONV. The protocols applied in the prevention of PONV include many parameters such as a short fasting period, early mobilization, early oral intake, avoidance of emetogenic agents such as opioids, and administration of PONV-preventing medications when necessary [26]. Although limiting the use of opioids as much as possible is recommended in ERAS protocols, the issue of opioid use in surgeries with intense postoperative pain such as thoracotomy is still controversial [27, 28]. Local anesthetics and opioids can be used alone or in combination for TEA infusions. Local anesthetics alone can often be associated with hypotension due to vasodilation and further motor and sensory blockade. Opioids may be added to reduce sympathectomy. However, epidurally administered opioids may show side effects similar to systemic opioids, such as long-term postoperative ileus and nausea [28, 29]. We planned our study retrospectively and analyzed the data of patients who underwent standard anesthesia and postoperative analgesia protocol in the groups with and without PONV. The initiation of thoracic epidural infusion before the surgical incision and its continuation in the postoperative period provided a limited need for rescue analgesia.

There are some limitations to our study. Since the study was retrospective, data such as the history of motion sickness, history of PONV, and smoking habits of the patients could not be analyzed properly. Additionally, the small number of patients with PONV negatively affects the power analysis of the results. Detailed prospective studies on this subject will contribute to the incidence evaluation of PONV in thoracic anesthesia, determination of possible predictive factors, and solutions.

## Conclusion

Demographic data, laboratory parameters, and clinical characteristics were evaluated concerning their correlation with PONV in this study. It was observed that the frequency of PONV might increase in patients with low RDW levels. In addition, higher VAS values and ASA PS were also found to increase the risk of PONV in patients who underwent thoracotomy and were administered TEA.

## Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

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