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Anxiety evaluated by the Hospital Anxiety and Depression Scale as a predictor of postoperative nausea and vomiting: a pilot study

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ABSTRACT

The incidence of postoperative nausea and vomiting (PONV) remains high, and improving the accuracy of PONV prediction remains challenging. The primary aim of this study is to examine the impact of anxiety scores evaluated using the Hospital Anxiety and Depression Scale (HADS) on the PONV prediction model. We hypothesized that anxiety and depression, quantified using the HADS, could improve the accuracy of the PONV predictive model. This pilot study evaluated 100 patients. The HADS was conducted by a self-evaluation method before thoracoscopic surgery for lung tumors, and the anesthesia method was standardized. The criterion was whether the nurse in charge of the patient who complained of PONV assessed that drug administration was necessary. As the main analysis, the odds ratio of the HADS score for predicting PONV was evaluated using multivariable logistic regression models. Further, the receiver operating characteristic (ROC) curves of the model with the HADS score added to the variables of without-anxiety predictors and the model with the variables of without-anxiety predictors only were compared. The anxiety score was significantly higher in the PONV group than in the no PONV group (P = 0.021). For predictive accuracy, the model that included age, sex, smoking history, history of PONV, and anxiety score had a higher area under the ROC curve than did the model excluding the anxiety score (P = 0.021). In conclusion, the findings indicate that the HADS is worth investigating as a predictor of PONV.

Keywords: postoperative nausea and vomiting, anxiety, anesthesia, logistic models, thoracic surgery

Abbreviations:
AUCs: areas under the curve
HADS: Hospital Anxiety and Depression Scale
OR: odds ratio
PONV: postoperative nausea and vomiting

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INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the most unpleasant complications after surgery, preventing early mobilization, delaying discharge, and causing readmission.[1-3] Despite the widespread use of minimally invasive surgical procedures, regional anesthesia, non-narcotic analgesics, and non-cholinesterase muscle relaxant antagonists, PONV still occurs in approximately 30–50% of patients undergoing surgery, and the incidence of PONV in the high-risk group reaches up to 80%.[4] Reducing the incidence of PONV is essential to improving patient satisfaction, and accurate prediction and prophylactic dosing is important with respect to medical costs.[5]

The risk factors used to predict PONV include female sex, younger age, non-smoker status, surgery type, history of PONV/motion sickness, and opioid analgesia.[4,6] Proposed strategies to reduce the risk of PONV include the following: minimizing inhalation anesthetics, avoiding high doses of neostigmine, and reducing postoperative opioids through of regional anesthesia. In addition, prophylactic medication for PONV is recommended for high-risk patients.[5,7,8] Therefore, if PONV can be predicted with high accuracy by adding anxiety to the predictors, patients requiring prophylactic medication can be appropriately identified.

Rita et al have reported that PONV is more likely to occur in people with strong anxiety symptoms,[9] and several reports have suggested the effect of anxiety on PONV.[10-13] In addition, it has been reported that perioperative anxiety not only causes PONV, but also reduces patients' perioperative performance.[14,15]

The Hospital Anxiety and Depression Scale (HADS) is a method for quantifying anxiety and depression[16-19] and has been translated in several languages.[5,20,21] The HADS was selected for this study because it has a validated Japanese version and can be surveyed in a short self-assessment format.[20] The primary aim of this study was to examine the impact of the anxiety scores calculated from the Japanese version of the HADS on the PONV prediction model and to verify whether the HADS is worth investigating on a large scale. To reduce the impact of factors other than anxiety, we conducted a study on a population of patients undergoing a specific surgical procedure using a standardized anesthesia protocol.

METHODS

Study design and patients

This single-center pilot study was approved by the Institutional Review Board (authorization number: 20190225-10) of our hospital and was conducted according to the tenets of the Declaration of Helsinki 2013. Informed consent was obtained using a questionnaire. This study was enrolled in the University Hospital Medical Information Network (UMIN000048235).

Patients who were over 20 years old and underwent lung tumor resection with full thoracoscopic surgery or thoracoscopic-assisted surgery from April 2019 to January 2021 were included. Surgery for lung tumors was selected for this study as the surgical procedure and anesthesia protocols at the institution are standardized. The exclusion criteria were as follows: (1) inability to understand Japanese; (2) emergency surgery; (3) preoperative vomiting symptoms due to underlying disease; (4) allergy to local anesthetics; (5) reoperation; (6) switch to open chest surgery due to intraoperative findings; (7) taking antipsychotic drugs preoperatively; and (8) patients judged to be inappropriate by the doctor in charge of this study.

Preoperative questionnaire

The Japanese version of the HADS questionnaire was completed through self-evaluation

before surgery. The nurse in charge of the preoperative outpatient department administered the questionnaire. The anesthesiologist-in-charge, postoperative rounds team, patient, and postoperative nurse-in-charge were blinded to the results of the questionnaire, and the results were sealed up to 72 h postoperatively.[1]

Anesthesia protocol and postoperative treatment

Complete intravenous anesthesia with propofol in combination with epidural anesthesia or nerve block was administered.[22] The selection of regional anesthesia and the dose of intraoperative drug were decided by the anesthesiologist-in-charge. For epidural anesthesia, 0.167% levobupivacaine was used, with continuous administration fixed at 4 mL/h, and a 3 mL bolus was administered at ≥30-min intervals in case of pain. The epidural catheter was removed on postoperative day 3. For nerve block, an intercostal nerve block or serratus anterior muscle surface block was performed, and 20–40 mL of 0.25% levobupivacaine was used as a single dose. Standard monitoring (non-invasive arterial pressure, electrocardiogram, pulse oximetry) and bispectral index monitoring were performed. There was no anesthesia premedication, and a target-controlled infusion pump was used to adjust the flow rate of propofol with a bispectral index target of 40–60. Fentanyl, remifentanil, and rocuronium were used in combination for induction and maintenance of anesthesia. No gastric tube was placed.[23]

A radial artery cannula was placed for blood pressure monitoring and blood sampling. Sugammadex was used to antagonize muscle relaxation.[24] Diclofenac sodium was used at the end of surgery, and analgesia was managed with regular administration of acetaminophen every 8 h postoperatively for 2 days.[25] For patients with a pain numeric rating scale score of ≥4, continuous intravenous infusion of fentanyl (20 mcg/h) was started, and the flow rate was adjusted until the numeric rating scale score decreased to <4.[26] PONV prophylaxis was not administered before or during surgery because the prophylactic use of 5HT3 receptor antagonists and corticosteroids was yet to be approved by Japanese health insurance practice during the study period. Patients who complained of PONV were treated with metoclopramide as the first choice.

Evaluation

The observation period was within 72 h postoperatively, and the primary endpoint was the presence of PONV. If a patient complained of nausea and vomiting symptoms, metoclopramide was administered at the decision of the nurse in charge, and the patient was classified into the PONV group. Other cases were classified as the no PONV group. In addition, age, sex, height, weight, operation time, intraoperative fentanyl use, postoperative fentanyl use, HADS score, smoking history, and history of PONV were evaluated. Patient information was collected from the electronic medical record system, and the data were aggregated. Age, sex, smoking history, and history of PONV were defined as without-anxiety predictors, and the PONV predictive model created with without-anxiety predictors was defined as the without-anxiety predictive model.

Statistical analyses

We planned to collect 100 samples. Given that this was a pilot study, a statistical sample size design was not performed. Between-group comparisons of patient characteristics were performed using the Mann–Whitney *U* test and chi-square test with Yates' continuity correction for continuous and categorical variables, respectively. As for the main analysis, the odds ratio of the HADS score for predicting PONV was evaluated using a multivariable logistic regression model adjusted by fixed variables from the without-anxiety predictors. In addition, the predictive value of the HADS score was evaluated by comparing the receiver operating characteristic (ROC) curves between the model that included the HADS score in the variables of without-anxiety predictors

and the model that included the variables of without-anxiety predictors only. The difference in areas under the curve (AUCs) of ROC curves was tested using Delong's test. As an additional assessment, we performed a 5-fold cross-validation to evaluate the generalization error of the model with HADS added to the variables used in the without-anxiety predictive model. All statistical analyses were performed using Python version 3.9.12 (https://www.python.org/) and R version 4.2.1 (https://www.r-project.org/). The significance level was set at 5% for all analyses.

RESULTS

Patient characteristics

Among the 100 patients evaluated, 2 patients were excluded because of discontinuation of surgery (N = 1) and reoperation (N = 1). Finally, 98 patients were included in the analysis. All 98 patients completed the questionnaire and were monitored for PONV within 72 h postoperatively (Fig. 1). No patient had anxiety or depression as an underlying diagnosis. All patients received regional anesthesia, and any patient with contraindications to metoclopramide was not included. The results of the Mann–Whitney *U* test or chi-square test with Yates' continuity correction are shown in Table 1. The PONV and no PONV groups involved 22 (22.4%) and 76 (77.6%) patients, respectively. The PONV group had significantly more females (N = 17/22 in the PONV group vs N = 18/76 in the no PONV group, $P < 0.001$). In addition, there were significant differences in smoking history ($P < 0.001$), height ($P < 0.001$), and weight ($P = 0.002$). The anxiety score was significantly higher in the PONV group ($P = 0.021$), but there was no significant difference in the depression score ($P = 0.394$). Intraoperative fentanyl usage was also not significantly different ($P = 0.117$); a total of 7 patients (7.1%) needed postoperative fentanyl.

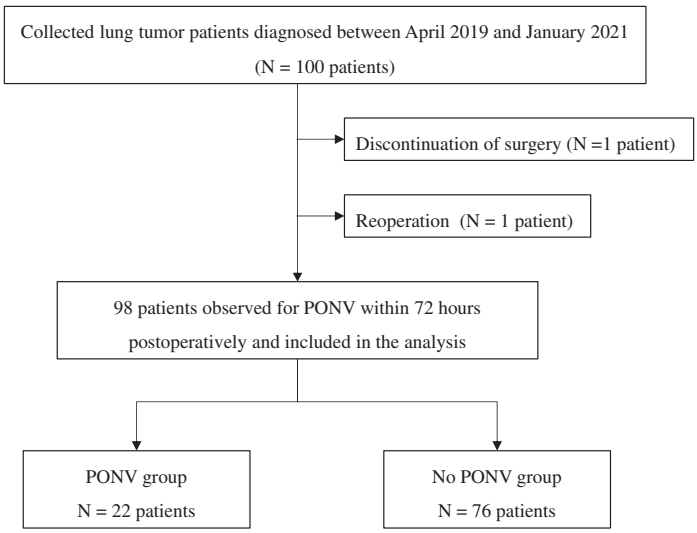

Fig. 1 Study flowchart

The Japanese version of the HADS questionnaire was distributed at the preoperative outpatient department, and 100 patients who responded were included. One patient was excluded because of postponement of surgery, and another patient was excluded as the procedure was a reoperation. A total of 98 patients were thus included in the study and observed for 72 hours postoperatively.

HADS: Hospital Anxiety and Depression Scale

PONV: postoperative nausea and vomiting

Table 1 Patient characteristics and outcomes by group

Characteristic	PONV group (N=22)	No PONV group (N=76)	P value
Age (years)	73 [61–78]	72 [67–75]	0.682
Sex (female, N (%))	17 (77.3%)	18 (23.7%)	<0.001
Height (cm)	153.4 [149.9–159.8]	161.0 [157.1–167.8]	<0.001
Weight (kg)	54.0 [46.4–59.3]	60.1 [55.4–65.0]	0.002
Body mass index (kg/m^2)	21.9 [20.7–23.5]	22.9 [20.6–24.9]	0.263
Anxiety score[a]	6.5 [4.0–9.8]	4.0 [2.0–7.0]	0.021
Depression score[a]	6.0 [2.5–8.0]	4.0 [2.0–8.0]	0.394
Operation time (min)	113.5 [83.3–139.8]	131.5 [92.3–148.3]	0.252
Smoking history	6 (27.3%)	56 (73.7%)	<0.001
Fentanyl (mcg/kg)[b]	6.7 (5.0–8.1)	6.2 (4.9–7.3)	0.117
Need postoperative fentanyl[c]	1 (4.5%)	6 (7.9%)	0.946
History of PONV	2 (9.1%)	5 (6.6%)	>0.999

Data are reported as number (%) or median [interquartile range, Q1–Q3].
Characteristics were compared between patients with and without PONV using Mann-Whitney *U* test and chi-square test with Yates' continuity correction.
PONV: postoperative nausea and vomiting
[a]Anxiety and depression scores were quantified using the Hospital Anxiety and Depression Scale.
[b]Intraoperative fentanyl use.
[c]The number of patients who required postoperative fentanyl.

Table 2 shows the results of multivariable logistic regression analysis. We compared the without-anxiety predictive model using age (odds ratio [OR]: 0.989; P = 0.704), sex (female; OR: 6.509; P = 0.017), smoking history (smoker; OR: 0.412; P = 0.253), and history of PONV (OR: 1.381; P = 0.775) with the predictive model including anxiety score (OR: 1.220; P = 0.018). The AUC of the without-anxiety predictive model was only 0.77, while the AUC of the predictive model that included the HADS anxiety score was 0.85. This indicated that the predictive model that included the HADS anxiety score was more accurate (P = 0.021) (Fig. 2). In addition, when the data of this study were cross-validated using the predictive model that included the HADS anxiety score, the AUC was 0.82 (Fig. 3).

Table 2 Multivariable logistic regression model of risk factors for PONV

Variable	Odds ratio	95% CI	P value
Anxiety score[a]	1.220	1.041–1.452	0.018
Age (years)	0.989	0.932–1.052	0.704
Sex (female)	6.509	1.459–33.439	0.017
Smoking history (smoker)	0.412	0.087–1.940	0.253
History of PONV	1.381	0.125–11.934	0.775

PONV: postoperative nausea and vomiting
CI: confidence interval
[a]Anxiety score was quantified using the Hospital Anxiety and Depression Scale.

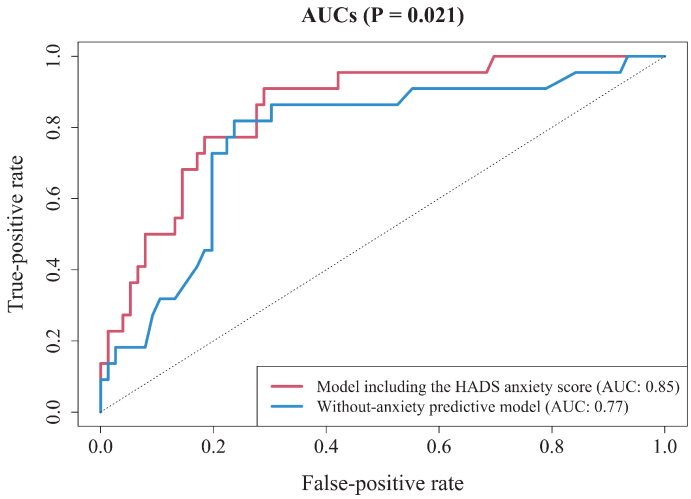

Fig. 2 Comparison of AUCs of receiver operating characteristic curves for the without-anxiety predictive model and the predictive model including anxiety score

The difference in AUCs was tested using Delong's test (P = 0.021). The without-anxiety predictive model included age, sex, smoking history, and history of PONV, and the predictive model included the anxiety score.

AUCs: areas under the curve

HADS: Hospital Anxiety and Depression Scale

PONV: postoperative nausea and vomiting

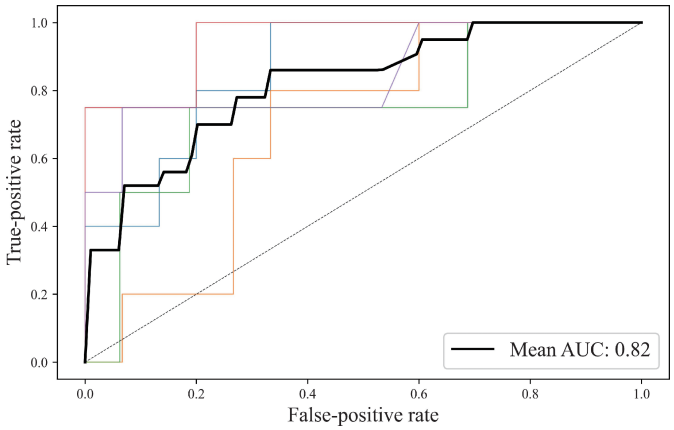

Fig. 3 Cross-validation using the predictive model including the HADS anxiety score

In the 5-fold cross-validation of the study data, the predictive model that included the anxiety score had an AUC of 0.82. The predictive model included the anxiety score in addition to age, sex, smoking history, history of PONV, and anxiety score.

AUC: area under the curve

HADS: Hospital Anxiety and Depression Scale

PONV: postoperative nausea and vomiting

DISCUSSION

Anxiety has been reported to be a risk factor for PONV, but it has not yet been evaluated as a risk assessment item for PONV.[4] The impact of anxiety assessed by the HADS on PONV prediction is not clear. This study revealed that, under specific conditions, anxiety scores assessed by the HADS can be predictive of PONV. In addition, it has not yet been proven that the inclusion of anxiety improves the predictive accuracy of PONV; thus, it is worthwhile to validate the HADS as a predictor on a large scale.[27,28]

The current study found a significant difference in anxiety scores between the PONV and no PONV groups. There were also significant differences in sex, height, weight, and smoking history. These results suggest that sex, anxiety score, and smoking history are risk factors for PONV. Multivariable logistic regression analysis using age, sex, smoking history, history of PONV, and anxiety score showed that the model that included the HADS anxiety score had an odds ratio of 1.220, and the P value was 0.018. These results support that the anxiety score is a risk factor for PONV. Notably, although there was a significant difference in anxiety scores between the two groups, there was no significant difference in the depression score, suggesting that the classification between anxiety and depression may be important.

Data from this study were evaluated with the predictive model that included the HADS anxiety score, and the AUC was 0.85. Meanwhile, the AUC of the predictive model that excluded the HADS anxiety score was lower at 0.77. When these AUCs were evaluated using Delong's test, the P value was 0.021, indicating the superiority of the predictive model that included the HADS anxiety score. In a previous study, the predictive model that included sex, history of PONV, smoking history, and postoperative opioids had an AUC of 0.67, while the predictive model that excluded postoperative opioids but included age, surgery type, and anesthesia method had an AUC of 0.72.[10]

In another study, the predictive model using age, sex, history of PONV, and postoperative opioids had an AUC of 0.64, while the predictive model in which surgery type, operation time, and anesthesia method were added was 0.71.[29] In the current study, the sample size for developing the predictive model was small (98 cases), and we performed cross-validation of five divisions to evaluate the generalization error of the predictive model that included the anxiety score. The mean AUC was 0.82. In a study using an independent validation set with the predictive model including age, sex, smoking history, history of PONV, anesthesia method, anesthesia time, and surgery type, the AUC was 0.79; however, this study included information that cannot be obtained before surgery.[30]

There are some limitations to this study. First, the decision to administer metoclopramide for PONV was based on the nurse in charge of the patient, and there may be subjective bias. Second, the patient's history of motion sickness could not be accurately ascertained, and therefore, the previously noted factors were missing. Third, because the study included patients with lung tumors, there were many smokers, with 63.3% of all patients having a history of smoking. Although smoking was an important risk factor and predictor of PONV, the results of this study were from a population with a high smoking rate. Forth, patients with an overall low anxiety score were included because patients with underlying anxiety disorders were excluded. Finally, because this was a pilot study, sample size calculations were not performed.

In conclusion, it would be worthwhile to conduct a larger HADS study to explore whether the accuracy of PONV predictions could be improved.

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COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

FINANCIAL DISCLOSURE

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

ETHICS APPROVAL

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board (authorization number: 20190225-10) of Ogaki Municipal Hospital.

CONSENT TO PARTICIPATE

Informed consent was obtained using a questionnaire from all individual participants included in the study.

CONSENT TO PUBLISH

No patient-identifying images are included in this study.

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