



Original Contribution

# Dose of intraoperative remifentanil administration is independently associated with increase in the risk of postoperative nausea and vomiting in elective mastectomy under general anesthesia



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## Abstract

**Background:** Postoperative nausea and vomiting (PONV) is one of the common complications in patients who have undergone surgery with general anesthesia. The association of intraoperative use of remifentanil with PONV has remained controversial. The aim of the current study was to determine the association of dose of intraoperative remifentanil administration with incidence of PONV.

**Methods:** The present study was a single-center retrospective observational study and included 423 female patients with American Society of Anesthesiologists physical status I or II who underwent elective mastectomy under general anesthesia between October 2011 and October 2012. The incidence of PONV within 3 days after the operation was prospectively assessed. The time-weighted average of remifentanil during the operation (twRem) was calculated. We used a multivariate regression model to assess the independent association of the twRem with the incidence of PONV.

**Results:** Among 423 patients, 129 patients (30.5%) had PONV during the study period. Remifentanil was administered in 355 patients (83.9%). In the multivariate logistic regression model using categories of twRem, we found that increased twRem was independently associated with increase in the risk of PONV ( $P = .01$ ). There was an independent association between twRem greater than 0.2  $\mu\text{g}/\text{kg}$  per minute and increase in the risk of PONV.

**Conclusion:** This retrospective observational study revealed a dose-dependent association between dose of intraoperative remifentanil administration and increase in the risk of PONV. Time-weighted average of remifentanil greater than 0.2  $\mu\text{g}/\text{kg}$  per minute was independently associated with risk of PONV.

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## 1. Introduction

Postoperative nausea and vomiting (PONV) is one of the common complications in patients who have undergone

surgery with general anesthesia and may increase patient discomfort and costs [1].

Remifentanyl is an opioid with rapid clearance that is used for general anesthesia. Although the use of an opioid is a risk factor for PONV [2], the association between the use of remifentanyl and the incidence of PONV is not clear. In some studies, the administration of remifentanyl was associated with a decreased incidence of PONV [3,4], whereas it was shown to be associated with an increased incidence of PONV in other studies [5,6]. This discrepancy in results may be due to differences in the cases and doses of remifentanyl. However, there is little information on the association of difference in the dose of remifentanyl with incidence of PONV.

Accordingly, we conducted a retrospective observational study to assess the dose-dependent association of the use of remifentanyl with the incidence of PONV. The null hypothesis of this study is that there is no dose-dependent association of administration of remifentanyl and incidence of PONV.

## 2. Materials and methods

### 2.1. Study design

This study was a single-center retrospective observational study. The Ethics Committee of the National Cancer Center approved this investigation. The committee waived the need for informed consent for studies involving the use of the database.

### 2.2. Patients

All female patients who underwent elective mastectomy under general anesthesia between October 2011 and October 2012 were included in this study. We excluded patients with American Society of Anesthesiologists (ASA) physical status III or higher.

### 2.3. Primary outcome

The primary outcome was incidence of PONV that occurred within 3 days after the operation. We defined PONV as a presence of either nausea or vomiting. In study hospital, it was routine for nurses to assess and record nausea and vomiting every 8 hours for all postoperative patients during postoperative 3 days. Accordingly, we retrospectively collected the presence of PONV from electrical medical records. If patients had discharged hospital within postoperative 3 days, the incidence of PONV was assessed solely during hospital stay.

### 2.4. Dose of remifentanyl

We defined the dose of intraoperative remifentanyl as its time-weighted average (twRem): (total intraoperative dose of remifentanyl)/(body weight)/(anesthetic time) (micrograms per kilogram per minute).

#### 2.4.1. Patients' demographics

We obtained patients' information including information on age, weight, ASA physical status, operation time, anesthesia time, amount of bleeding, amount of intraoperative fluid infusion, intraoperative urinary output, intraoperative use of an inhalation anesthetic, nitrous oxide, dexamethasone, metoclopramide and flurbiprofen, and total dose of intraoperative fentanyl administration.

#### 2.4.2. Standard anesthesia

No premedication was given to any of the patients. Anesthesia was induced with propofol at 1 to 2 mg/kg, rocuronium at 0.6 mg/kg, and fentanyl at 1 to 2  $\mu$ g/kg or remifentanyl at 0.3 to 0.5  $\mu$ g/kg per minute to facilitate tracheal intubation. Anesthesia was maintained by sevoflurane inhalation or propofol infusion with fentanyl and/or remifentanyl. Epidural anesthesia was not used in any of the patients. Nonsteroidal anti-inflammatory drugs and pentazocine were used for postoperative analgesia as necessary.

## 2.5. Statistical analysis

Data are presented as percentages (n) or as medians (25% quartile, 75% quartile) because continuous data used in this study were not normally distributed. Comparisons among groups were conducted using the  $\chi^2$  test for equal proportion, Mann-Whitney *U* test, or Kruskal-Wallis test.

We first separated patients into groups with and without PONV. We compared the values of twRem in the 2 groups. We also compared their demographics to assess possible confounders for the association between twRem and incidence of PONV. To determine the independent association of remifentanyl dose with incidence of PONV, we constructed multivariate models using potential predictors of the incidence of PONV (criteria for inclusion at  $P = .2$ ). Results from the multivariate models are shown using odds ratios with 95% confidence intervals (CIs). Because the relationship between twRem and incidence of PONV may not be linear in nature, we separated patients into 4 subgroups according to each 0.5  $\mu$ g/kg per minute of twRem. This categorization was planned before analysis. We further performed multivariate logistic analysis using these categories of twRem.

All statistical analyses were performed using commercially available statistical software (SPSS 19.0; SPSS, Inc, Chicago, IL). Data were reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [7].

## 3. Results

During the study period, there were 423 female patients with ASA status I or II who underwent elective mastectomy under general anesthesia. We included all of them in this study. There were no missing data from these patients.

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