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Can Postoperative Nausea and Vomiting Be Predicted?

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Background: **Retrospective[1] studies fail to identify predictors of postoperative nausea and vomiting (PONV). The authors prospectively studied 17,638 consecutive outpatients who had surgery to identify these predictors.**

Methods: **Data on medical conditions, anesthesia, surgery, and PONV were collected in the post-anesthesia care unit, in the ambulatory surgical unit, and in telephone interviews conducted 24 h after surgery. Multiple logistic regression with backward stepwise elimination was used to develop a predictive model. An independent set of patients was used to validate the model.**

Results: **Age (younger or older), sex (female or male), smoking status (nonsmokers or smokers), previous PONV, type of anesthesia (general or other), duration of anesthesia (longer or shorter), and type of surgery (plastic, orthopedic shoulder, or other) were independent predictors of PONV. A 10-yr increase in age decreased the likelihood of PONV by 13%. The risk for men was one third that for women. A 30-min increase in the duration of anesthesia increased the likelihood of PONV by 59%. General anesthesia increased the likelihood of PONV 11 times compared with other types of anesthesia. Patients with plastic and orthopedic shoulder surgery had a sixfold increase in the risk for PONV. The model predicted PONV accurately and yielded an area under the receiver operating characteristic curve of 0.785 ± 0.011 using an independent validation set.**

Conclusions: **A validated mathematical model is provided to calculate the risk of PONV in outpatients having surgery. Knowing the factors that predict PONV will help anesthesiologists determine which patients will need antiemetic therapy. (Key words: Ambulatory anesthesia; ambulatory surgery; mathematical model.)**

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POSTOPERATIVE nausea and vomiting (PONV) remains one of the most common and distressing complications after outpatient surgery,[1] resulting in pain, hematoma, and wound dehiscence, which require additional resources and may delay discharge. Patients with persistent PONV in the ambulatory surgical unit (ASU) continue to have an increased risk of postoperative symptoms 24 h after surgery[2] and to be impaired in performing their normal daily activities.[3] Of further concern, PONV increases the likelihood of unanticipated admission after ambulatory anesthesia by approximately three to four times.[4,5]

To maintain the efficiency and cost-saving benefit of ambulatory surgery, effective antiemetic administration and prophylaxis for certain patients having outpatient surgery would be desirable. A quantitative identification of the factors associated with PONV would make it easier to target specific patients for effective therapy. Several studies have outlined the factors related to an increased incidence of PONV.[6–9] However, most of these studies are retrospective. The degree to which these factors are predictors of PONV remains unknown. Using a large population, our objective was to characterize the incidence rate of PONV and to determine the predictive factors that increase the risk for PONV. In addition, we have developed and validated a mathematical model to calculate the risk for PONV in this population of patients.

Materials and Methods

Preoperative and Intraoperative Data Collection

After our institutional ethics committee approved our study, we studied 17,638 consecutive ambulatory surgical patients prospectively studied during a 3-yr period at the ASU of The Toronto Hospital, Western Division. Written informed consent was not required by the ethics committee for the study. Verbal consent for a telephone interview 24 h after operation was obtained. The patients were 5,812 men and 11,826 women, with a mean (± SD) age of 46.7 ±

21.2 yr. Preoperative patient characteristics and intraoperative variables were documented on specifically designed, standardized adverse-outcome check-off forms. Data on demographics, preoperative medical conditions, American Society of Anesthesiologists (ASA) status, duration of anesthesia, surgical procedure, and intraoperative management (drugs, techniques, monitoring, and so on) were documented in the anesthesia record.

Postoperative Data Collection

The patients received standardized monitoring of pulse rate, blood pressure, pulse oximetry, level of consciousness, respiratory rate, and temperature on arrival in the post-anesthesia care unit (PACU). The patients received (intravenously) 2–4 mg morphine for pain relief and 25–50 mg dimenhydrinate for nausea or vomiting. Patients were discharged to the ASU when their Aldrete scores[10] were 9 or more. Post-anesthesia discharge scores[11] were maintained, and the patients were discharged when their scores were 9 or more.

The duration of surgery and the time spent in the PACU and the ASU were recorded. The assessment score on admission and discharge, medication given, physiologic variables, and discharge location were recorded in the PACU and ASU nursing records.

The PACU nursing staff scored PONV on the standardized adverse outcome check-off forms. Nausea or vomiting in the ASU and reported at the 24-h telephone interview was scored on the standardized adverse outcome check-off forms by ASU nursing staff. The definition of PONV was printed on the forms. In the PACU and ASU, PONV was defined as any volunteered report of nausea or observed active retching or vomiting requiring antiemetics.

Patient charts were completed on discharge, and the data were reviewed systematically the next day by a research assistant and an experienced anesthesiologist. The data were coded for computer entry. The surgical procedure was converted into the corresponding International Classification of Diseases (ICD9CM) procedure code and subsequently recorded in eight groups: orthopedic surgery; urology; general surgery; plastic surgery; neurosurgery; ear, nose and throat (ENT) and dental surgery; gynecology; and ophthalmology.

Postoperative Telephone Interviews

Telephone interviews were conducted 24 h after the surgery by ambulatory surgical nurses trained in research interviewing, using a standardized questionnaire. Patients were not interviewed if they had refused to give consent to the telephone interview before operation, if they did not speak English, or if they could not be reached on two attempts.

Statistical Analyses

Descriptive statistics on patient, surgery, and anesthesia characteristics are given in frequencies and percentages. Mean doses of anesthesia-related drugs were calculated and compared between patients with and without PONV using the Student *t* test. To describe associations between PONV and various patient, surgical, and anesthesia characteristics, we first performed univariate analyses. The frequency of PONV in the PACU, the ASU, and at home within 24 h was compared among groups of patients with different characteristics. For categorical variables, chi-squared statistics were determined to estimate statistical significance. For continuous variables, the Student *t* test was used to compare mean values of variables between groups of patients with and without PONV.

To identify independent predictors for PONV, we used multiple logistic regression with backward stepwise elimination. To validate our final statistical model, we randomly divided our patient population into two equal halves: a model development set and a model validation set. The development set was used to develop our statistical model for PONV prediction. The following variables were entered into the logistic model at the first step of the backward elimination. Age (in yr), body mass index (in kg/m^2), and duration of procedure (in min) were continuous variables. Sex, ASA physical status, type of anesthesia, type of surgery, smoking status, and history of previous PONV were categorical (dummy) variables. We report the final model. To enable the reader to calculate the risk of PONV for patients based on their characteristics, the entire final model is reported in appendix 1.

Using the final model obtained from the development set, the probability of PONV was calculated for each patient in the validation set. Based on these calculated (predicted) probabilities and the patients' actual experiences in the validation set (*i.e.*, whether PONV occurred), a receiver operating characteristic (ROC) curve was plotted using 100 cut points. The area under the ROC curve was calculated according to a method given by Hanley and McNeil.[12] The area under the ROC curve was used as a measure of accuracy of the final prediction model.

The patients in the validation set were grouped by their calculated probabilities of PONV into 10 risk percentiles. The observed frequency of PONV in these 10 percentiles was plotted against the median of the predicted probability in the corresponding risk groups. The Pearson correlation coefficient was calculated to determine how well the median predicted probabilities correlated with the observed frequencies. All statistical analyses were performed using SAS Statistical Software, version 6.12 (SAS Institute, Cary, NC).

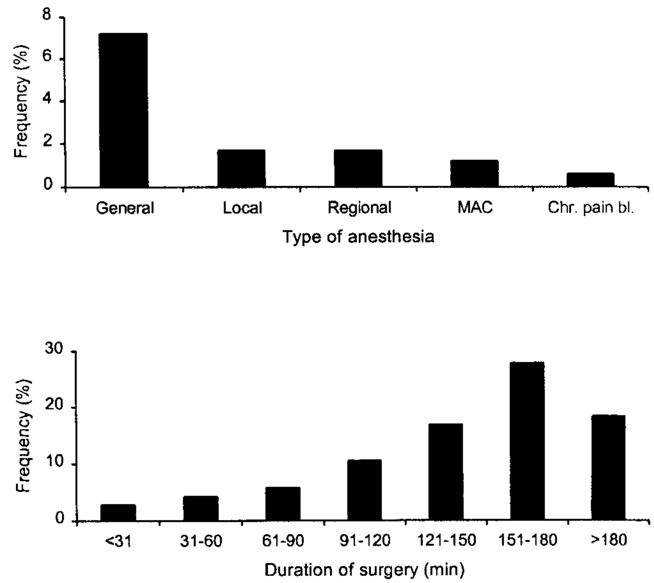

Fig. 1. The frequency of nausea and vomiting by type of anesthesia and duration of surgery. MAC = monitored anesthesia care.

Results

Of the 17,638 patients enrolled, two thirds were women and more than 90% were classified as ASA physical status I or II (table 1). There was a wide age range, with a mean of 46.7 ± 21 yr. Overall, 816 patients (4.6%) experienced PONV in the PACU or ASU. Women had a nearly twofold higher rate of PONV in both the PACU and ASU compared with men. Higher rates of PONV were observed among ASA I and II patients than among ASA III patients. Among patients younger than 50 yr, there was no association between age and the frequency of PONV. However, among patients older than 50 yr, the frequency of PONV showed a marked linear decrease with increasing age. Patients with PONV were significantly younger than patients without PONV (38 ± 16 yr *vs.* 47 ± 21 yr, $P < 0.0001$).

More than 90% of the patients received general anesthesia (n = 10,110) or monitored anesthesia care (n = 6,301). There was a fivefold increase in the risk of PONV among patients receiving general anesthesia compared with other types of anesthesia (fig. 1). Most of the procedures (93.6%) lasted less than 90 min, with an average duration of 52 ± 44 min. Except for the procedures that lasted more than 3 h, there was a direct association between the duration of anesthesia and the incidence of PONV. The frequency increased from 2.8% among patients with surgical duration ≤ 30 min to 27.7% among patients with surgery lasting 151–180 min.

Table 1. Frequency of Postoperative Nausea and Vomiting by Patient Characteristics

	No.	Frequency in PACU (%)	Frequency in ASU (%)	Combined Frequency (%)
Total	17,638	2.2	3.0	4.6
Sex				
Male	5,812	1.3	2.3	3.3
Female	11,826	2.6	3.3	5.3
ASA status				
I	9,194	2.5	3.5	5.3
II	7,301	1.9	2.5	4.1
III	1,143	1.3	1.2	2.5
Age (yr)				
≤20	1,429	3.3	3.6	6.3
21–30	3,873	2.9	3.5	6.1
31–40	3,319	3.2	4.2	6.5
41–50	1,944	2.6	4.5	6.4
51–60	1,539	1.5	2.9	4.0
61–70	2,060	1.0	1.7	2.5
71–80	2,296	0.7	0.8	1.4
81–90	1,110	0.5	0.6	0.8
≥90	68	0	0	0

There was a wide variation in the incidence of PONV according to the type of surgery (table 2). Patients undergoing ENT or dental surgery had the highest incidence (14.3%), followed by patients with orthopedic (7.6%) and plastic surgery (7.4%). Patients having urologic, gynecologic, neurologic, or general surgery had an incidence of PONV corresponding to the overall average (4%–5.2%). Patients undergoing ophthalmologic procedures and chronic pain block experienced the lowest incidence of PONV (2.7% and 0.6%, respectively). There was, however, wide variation among the different procedures of the same surgical specialties. Among orthopedic patients, those undergoing shoulder surgery experienced the highest frequency of PONV (16.6%). Patients undergoing breast augmentation experienced an 8- to 10-fold higher incidence than did those undergoing other types of plastic surgery. Among women having gynecologic surgery, the frequency of PONV was significantly greater in those undergoing laparoscopic sterilization, diagnostic laparoscopy, or hysteroscopy. Among

Table 2. Frequency of Postoperative Nausea and Vomiting by Surgical Procedure

Surgical Procedure	No.	Frequency in PACU (%)	Frequency in ASU (%)	Combined Frequency (%)
ENT/dental	224	7.1	8.9	14.3
Dental	16	0	25.0	25.0
ENT	208	7.7	7.7	13.5
Orthopedics	3,179	3.0	5.4	7.6
Shoulder	411	6.3	12.9	16.6
Hand, wrist	263	3.4	5.7	8.0
Hardware removal	207	1.5	6.3	7.7
Knee	1,898	2.6	4.2	6.3
Ankle	220	3.2	2.3	4.6
Elbow	88	0	4.6	4.6
Hip and other	92	0	4.4	4.4
Plastic surgery	633	3.3	4.9	7.4
Breast augmentation	41	22.0	26.8	41.5
Skin and other	153	2.6	3.3	5.9
Face	96	0	5.2	5.2
Hand	343	2.3	2.9	4.7
Urologic	232	1.3	3.9	5.2
Testicle/scrotum	29	3.5	6.9	10.3
Bladder/prostate/kidney	174	1.2	4.0	5.2
Circumcision	29	0	0	0
Gynecologic	5,959	2.7	2.2	4.6
Laparoscopy (sterilization)	325	9.5	10.8	17.5
Hysteroscopy	221	7.7	6.3	11.3
Laparoscopy (diagnostic)	415	3.9	6.0	9.2
Biopsy/repair	50	2.0	8.0	8.0
D&C (diagnostic)	290	1.4	2.1	3.5
D&C (abortion)	4,658	2.0	1.1	3.0
Neurosurgery	484	2.3	2.7	4.3
Nerve decompression, repair	171	4.7	5.9	8.8
Carpal tunnel	313	1.0	1.0	1.9
General surgery	398	1.5	3.3	4.0
Varicose vein stripping	9	0	22.2	22.2
Skin	52	3.9	9.6	9.6
Breast	221	1.4	2.3	3.6
Other	106	0.9	0.9	0.9
Anal	10	0	0	0
Ophthalmologic	6,372	1.0	2.0	2.7
Strabismus	423	9.2	15.8	22.0
Other	514	1.4	2.7	3.3
Cornea	423	0.5	1.2	1.7
Cataract	4,700	0.4	0.9	1.1
Trabeculectomy	312	0	1.0	1.0
Chronic pain block	157	0.6	0	0.6
Total	17,638	2.2	3.0	4.6

the relatively low-risk ophthalmologic patients, those undergoing strabismus surgery had a 10-fold higher frequency of PONV than did other patients having ophthalmologic procedures. The frequency of PONV was related to the degree of postoperative pain. Among patients experiencing excessive postoperative pain, the frequency of PONV was 16.1%, whereas 3.9% of the patients without excessive pain experienced PONV ($P <$ 0.0001).

Patients with PONV underwent significantly longer procedures (67 ± 57 min *vs.* 51 ± 44 min; $P < 0.0001$), and the duration of their stay in the PACU (72 ± 32 min *vs.* 49 ± 25 min; $P < 0.0001$) and the ASU (157 ± 84 min *vs.* 95 ± 53 min; $P < 0.0001$) was also significantly longer (fig. 2).

Among patients undergoing general anesthesia, those who experienced PONV during the immediate postoperative period had received significantly higher doses of alfentanil, fentanyl, and midazolam during operation (table 3). The same was true of those who received monitored anesthesia care. Patients experiencing PONV received significantly higher doses of dimenhydrinate in the PACU and ASU (37 ± 19 mg *vs.* 23 ± 11 mg; $P <$ 0.0001). Among patients who received general anesthesia, those with PONV within 24 h after surgery received significantly higher doses of morphine in the PACU and ASU than did those without PONV (6.3 ± 3.6 mg *vs.* 5.3 ± 3.5 mg; $P = 0.008$).

Among patients undergoing general anesthesia, 1,225 (12%) received a nondepolarizing muscle relaxant during operation. Five hundred patients (41%) received a reversal agent (483 received neostigmine, 17 received edrophonium) at the end of the procedure. There was no significant difference in PONV between those who received a reversal agent and those who did not (19.2% *vs.* 15.7%; $P = 0.11$).

For the 24-h postoperative telephone interview, 5,264 patients responded (29.8%). Of the nonrespondents, 5,878 (33.3%) refused to give an interview, 2,169 (12.3%) did not speak English, and 4,327 (23.6%) could not be contacted. There was no significant difference between respondents and nonrespondents in the mean

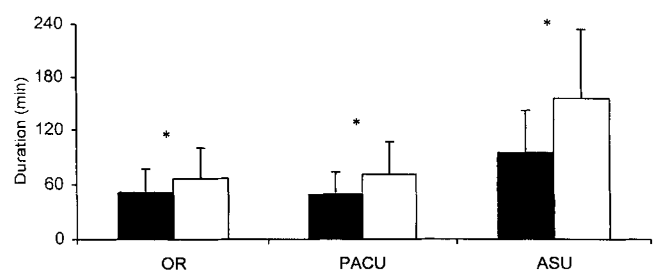

Fig. 2. The mean duration of anesthesia (OR) and the duration of stay in the postanesthesia care unit and ambulatory surgery unit for patients with (*open bars*) or without (*solid bars*) postoperative nausea and vomiting. Asterisks indicate a significant difference ($P < 0.05$).

Table 3. Frequency of Postoperative Nausea and Vomiting by Intraoperative Anesthetic Drug Dose

	Nausea or Vomiting in PACU or ASU	
Drug	Yes	No
General anesthesia		
Alfentanil (μg)	964 ± 718 (131)*	683 ± 524 (1,959)
Fentanyl (μg)	107 ± 61 (578)*	83 ± 55 (6,884)
Sufentanil (μg)	10.0 ± 3.2 (6)	9.6 ± 3.6 (33)
Propofol bolus ind. (mg)	174 ± 45 (678)	177 ± 51 (8,927)
Thiopental (mg)	349 ± 146 (29)	327 ± 154 (149)
Midazolam (mg)	1.3 ± 0.6 (210)*	1.2 ± 0.6 (2,104)
Droperidol (mg)	0.8 ± 0.4 (83)	0.7 ± 0.4 (983)
Monitored anesthesia care		
Alfentanil (μg)	631 ± 292 (21)*	508 ± 269 (1,336)
Fentanyl (μg)	68 ± 30 (47)*	54 ± 28 (3,600)
Sufentanil (μg)	—	4.3 ± 2.5 (2)
Propofol neurolept (mg)	33 ± 37 (33)	24 ± 19 (3,550)
Midazolam (mg)	1.5 ± 0.9 (68)*	1.2 ± 1.2 (5,829)
Droperidol (mg)	0.9 ± 0.2 (2)	1.0 ± 0.5 (121)

Values are mean ± SD. Numbers of patients in each group are given in parentheses.

* $P < 0.05$, significantly different from patients without nausea or vomiting.

age (47 ± 20 yr *vs.* 47 ± 22 yr), duration of anesthesia (53 ± 39 min *vs.* 52 ± 47 min), or frequency of PONV in the PACU and ASU (4.6% *vs.* 4.6%). However, respondents had a higher body mass index (25.8 ± 5.2 *vs.* 25.3 ± 5.1 kg/m^2; $P < 0.0001$) and a longer duration of stay in the PACU (53 ± 24 *vs.* 50 ± 26 min; $P < 0.0001$) and in the ASU (103 ± 57 *vs.* 96 ± 56 min; $P < 0.0001$). There was a significantly lower response rate among ASA III patients than among healthier patients (26% *vs.* 30%; $P < 0.01$). There were significant differences in the response rate by type of surgery (chi-square$_{(8)}$ = 66.7; $P < 0.001$). There was a higher than average response rate among patients undergoing urologic (38%), general (37%), ENT or dental (33%), orthopedic (32%), or ophthalmologic surgery (31%), whereas patients undergoing gynecologic procedures or receiving chronic pain block were less likely to give an interview (27% and 17%, respectively). Patients had different response rates according to the type of anesthesia (chi-square$_{(4)}$ = 45.9; $P < 0.001$). There was a lower response rate among patients receiving regional (25%) or local (23%) anesthesia than among patients receiving monitored anesthesia care (32%) or general anesthesia (30%).

Among the respondents, 481 patients (9.1%) experienced PONV within 24 h after operation. Women experienced a higher rate of PONV within 24 h than did men (10% *vs.* 7.4%; $P = 0.002$), but there was no significant difference in the incidence by ASA status. Patients younger than 50 yr experienced a higher incidence (10.2%) of PONV than did older patients (6.7%). Patients receiving monitored anesthesia care had a lower frequency (6.2%). Except for procedures lasting more than 3 h, the incidence of PONV within 24 h increased with increasing duration of anesthesia.

The incidence of PONV showed less variation by surgical specialty within the first 24 h after operation than in the immediate postoperative period. However, the pattern remained similar: ENT or dental, plastic surgery, and orthopedic patients had the highest incidence (table 4). Of the specific procedures, patients undergoing breast augmentation and shoulder surgery experienced the highest incidence of PONV within 24 h (43% and 19%, respectively).

The characteristics of the development set and the validation set were similar. There were no significant differences between the two groups (table 5). Using multiple logistic regression with backward elimination including only the development set, we found that age, sex, smoking status, history of previous PONV, type and duration of anesthesia, and type of surgery were independent predictors of PONV (table 6). The ASA status was not a significant independent predictor. Age was inversely associated with the risk for PONV. A 10-yr increase in age was associated with a 13% decrease in the likelihood of PONV. Men had one third the risk for PONV compared with women. Smokers had two thirds the risk for PONV compared with nonsmokers. Patients with history of previous PONV had a threefold increase in the likelihood PONV compared with patients with no previous PONV. There was a direct association between the duration of anesthesia and the risk for PONV. A 30-min increase in duration predicted a 59% increase in the incidence of PONV. General anesthesia increased the likelihood of PONV 11 times compared with other types of anesthesia. The risk for PONV to develop among patients receiving monitored anesthesia care, local anesthesia, regional anesthesia, or chronic pain block was not significantly different. Compared with the reference group, which includes general surgery, gynecologic dilation and curettage (D&C), urologic surgery, neurosurgery, and chronic pain block, patients undergoing plastic surgery had a sevenfold increase in the risk for PONV. Patients undergoing orthopedic shoulder surgery, ophthalmologic, or ENT procedures had a four- to sixfold increase. Those undergoing orthopedic (nonshoulder) and gynecologic (non-D&C) procedures had a threefold increase in the risk for PONV.

To illustrate how the reported model can be used to estimate an individual patient's risk for PONV, we calcu-

Table 4. Frequency of Nausea and Vomiting by Surgical Procedure during the 24 h after Surgery

Surgical Procedure	No.	Frequency (%)
ENT/dental	73	16.4
ENT	67	17.9
Dental	6	0
Plastic surgery	181	14.4
Breast augmentation	14	42.9
Skin and other	36	16.7
Hand	96	11.5
Face	35	8.6
Orthopedic	1,013	14.3
Shoulder	73	19.2
Hip and other	27	18.5
Hand, wrist	76	18.4
Ankle	64	17.2
Elbow	22	13.6
Knee	680	13.1
Hardware removal	71	12.7
Neurosurgery	139	11.5
Nerve decompression, repair	37	16.2
Carpal tunnel	102	9.8
Chronic pain block	27	11.1
General surgery	149	10.7
Skin	16	18.8
Anal	8	12.5
Breast	107	10.3
Other	15	6.7
Varicose vein stripping	3	0
Urologic	87	9.2
Testicle/scrotum	10	10.0
Bladder/prostate/kidney	66	9.1
Circumcision	11	9.1
Gynecology	1,606	7.4
Biopsy/repair	11	18.2
Laparoscopy diagnostic	239	13.0
Laparoscopy sterilization	120	12.5
Hysteroscopy	98	11.2
D&C (diagnostic)	110	7.3
D&C (abortion)	1,023	5.0
Ophthalmologic	1,989	6.8
Strabismus	136	13.2
Cataract	1,454	6.7
Other	148	6.1
Cornea	131	5.3
Trabeculectomy	120	3.3
Total	5,264	9.1

lated the risk for PONV for five hypothetical patients (appendix 1).

Data from the validation set of patients were used to validate our final predictive model. The plotted ROC curve showed a fairly good overall accuracy of prediction (fig. 3). The area under the ROC curve was 0.785 ± 0.011. When we plotted the observed frequencies of PONV against the median predicted probabilities of the 10 risk percentiles, we found good linear correlation ($r^2 = 0.99$, $P < 0.0001$; fig. 4).

Discussion

In our study, the incidence of PONV was 4.6% in the PACU and ASU and 9.1% at the 24-h interview. A previous study of 143 ambulatory surgical patients found an increase in PONV 48 h after discharge (16.8%) compared with the incidence in the PACU (9.8%).[3] Because medications administered in the ambulatory surgery center undergo metabolism and elimination within 48 h after discharge, the increase in postdischarge PONV suggests a multifactorial cause related to early ambulation and resumption of oral intake.

The frequency of PONV in the PACU and ASU varied according to sex, ASA status, age, type and duration of anesthesia, type of surgery, and type of procedure within the same surgical specialty. The high frequency of PONV in the PACU and ASU (> 15%) among breast augmentation, strabismus repair, laparoscopic sterilization, varicose vein stripping, dental, and orthopedic shoulder procedures may justify the use of prophylactic antiemetics.

Patients undergoing breast augmentation had a 41.5% incidence of PONV in the immediate postoperative period and 42.9% 24 h after operation. The incidence of PONV in breast surgery has been reported to be 37–

Table 5. Patient Characteristics in the Development Set and the Validation Set

	Development Set (N = 8,819)	Validation Set (N = 8,819)
Age (yr)	47 ± 21	48 ± 21
Female/male (%)	67/33	67/33
ASA status I/II/III (%)	52/41/7	52/42/6
Type of anesthesia (%)		
General	58	57
Monitored anesthesia care	35	37
Local, regional, or chronic pain block	7	6
Type of surgery (%)		
Ophthalmology	36	37
Gynecology	34	33
Orthopedics	18	18
Other	12	12
Duration of anesthesia (min)	51 ± 27	52 ± 28
PACU stay (min)	50 ± 25	51 ± 25
ASU stay (min)	97 ± 55	98 ± 56
PONV (%)	4.5	4.8

Values are mean ± SD where appropriate.

Table 6. Predictive Factors from the Final Multiple Logistic Regression Model

Variable	Odds Ratio	95% Confidence Interval	*P* Value
Age 10 yr	0.87	0.8–0.9	0.0008
Sex (male/female)	0.36	0.3–0.5	0.0001
Smoking status (yes/no)	0.66	0.5–0.9	0.013
History of previous PONV (yes/no)	3.13	2.1–4.6	0.0001
Duration of anesthesia, 30 min	1.59	1.4–1.8	0.0001
General anesthesia	10.6	6.7–16.7	0.0001
Surgical procedure			
Plastic	6.68	3.5–12.6	0.0001
Orthopedics (shoulder)	5.91	3.4–10.3	0.0001
Ophthalmologic	5.85	3.8–9.0	0.0001
ENT	4.39	2.1–9.2	0.0001
Gynecologic (non-D&C)	3.31	2.3–4.8	0.0001
Orthopedic (knee)	2.82	1.9–4.2	0.0001
Orthopedic (other)	2.57	1.5–4.4	0.0006

Surgical procedures are compared with the reference group (urologic, general, and neurosurgery). General anesthesia is compared with all other types of anesthesia.

59%.[13,14] Further studies are needed to determine the cause of this apparently high incidence of PONV. Among the patients having orthopedic procedures, those undergoing shoulder surgery experienced the highest frequency of PONV (16.6%), possibly because of the high use of postoperative opioids. Ondansetron (8 mg) has been shown to be more efficacious than metoclopramide (10 mg) in reducing opioid-induced PONV.[15] Alternative pain treatment such as suprascapular nerve blocks[16] and ketorolac[17] may be helpful in reducing the use of postoperative opioids, thereby reducing the likelihood of PONV. Among the patients having ophthalmologic procedures, those undergoing strabismus surgery had a high incidence of PONV (22%). This may be caused by an oculocardiac reflex vagal response triggered by eye-muscle manipulation.[18]

Among the intraoperative anesthetic drugs, alfentanil and fentanyl were administered in significantly higher doses in patients with PONV. Although these doses do not demonstrate causality, the amount of narcotics may contribute to the incidence of PONV. Furthermore, patients with PONV stayed longer in the PACU and ASU (23 and 62 min, respectively). Despite a significantly higher

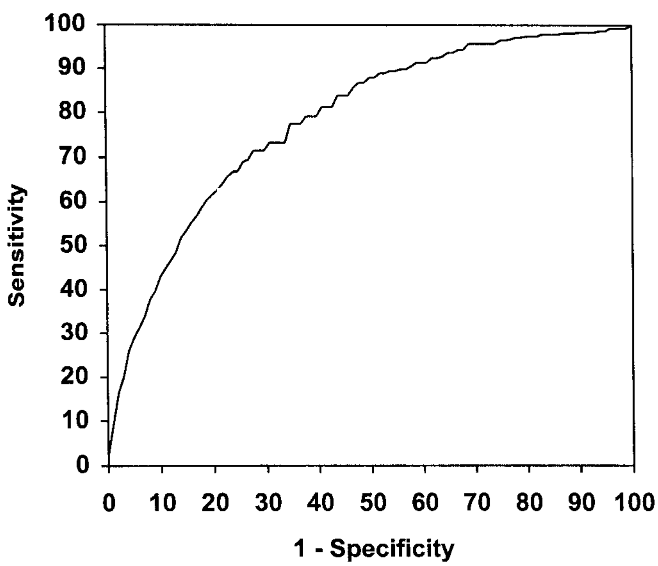

Fig. 3. The receiver operating characteristic curve for calculated probabilities of postoperative nausea and vomiting applied to the validation set of patients. The area under the curve = 0.785 ± 0.011.

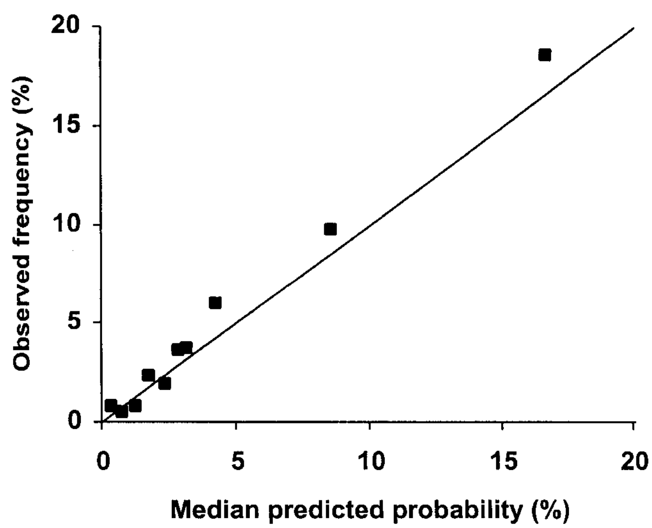

Fig. 4. The correlation between the median of the predicted probabilities and the observed frequencies of postoperative nausea and vomiting in the 10 risk percentiles (r^2 = 0.99, P < 0.001). The straight line represents perfect correlation.

dose of dimenhydrinate among these patients, it remains unclear whether this longer stay was due to the treatment of PONV. A decrease in PONV may reduce the duration of postoperative stay and increase the cost-effectiveness of the ASU. As an alternative or adjunct to opioids in the ambulatory surgery setting, nonsteroidal antiinflammatory drugs[16] should be considered for patients or surgical groups at high risk for PONV.

Among the 24-h respondents with PONV who received general anesthesia, morphine was administered in significantly higher doses in the PACU and ASU. Morphine's long duration of action may contribute to the high rate of PONV among these 24-h respondents. Further study is needed to determine the ideal timing of morphine administration in the ambulatory anesthesia setting.

In this study, sex, age, smoking, previous PONV, type and duration of anesthesia, and type of surgery were independent predictors of PONV. Men had one third the risk for PONV that women had. Previous reports supported this sex difference and attributed the finding to variations in serum gonadotropin or other hormone levels.[6-8,19]

Another predictor of PONV was age. Age decreased the likelihood of PONV by 13% for each 10-yr increase. Pioneer studies described a decreasing incidence among men with increasing age and an insignificant decrease among women until the eighth decade.[9] In contrast, our study showed a gradual decrease in PONV after age 50 yr. Interestingly, Koivuranta *et al.*,[20] using the forward procedure of logistic regression, did not find age to be a predictive factor for nausea, except for patients older than 50 yr who were undergoing joint replacement and spinal surgery, in whom there was an increased risk for postoperative vomiting.

Smoking was also a predictor of PONV. Smoking decreased the likelihood of PONV by 34%. The relation between smoking and PONV was not evident in the literature for many years. A multicenter study of anesthetic outcomes showed a lower risk for PONV in smokers (relative risk = 0.6).[21] Our results are consistent with recent studies that identified smoking as a protective factor against PONV.[20,22]

Another predictor of PONV is previous PONV, which increases the likelihood of PONV by three times. A recent study showed previous PONV as the second strongest predictor of PONV, in addition to a twofold increased risk for PONV among these patients.[20] Although an older study reports a 52-fold increased risk for PONV among patients with a history of PONV, its power is reduced by its small sample size.[23]

Anesthetic technique was also a predictor of PONV. Patients receiving general anesthesia were approximately 11 times more likely to experience PONV than were those who received monitored anesthesia care, regional anesthesia, or chronic pain block. PONV can be reduced by supplementing nitrous oxide and oxygen with propofol rather than a volatile gas.[24] Total intravenous anesthesia protects against PONV more than does general anesthesia with volatile agents.[25] Because our results apply to general anesthesia with volatile agents, further study is required to determine the predictive power of general anesthesia with intravenous agents.

The duration of anesthesia was another predictor of PONV, increasing the risk for PONV by 59% for each 30-min increase. This finding could be related to the larger number of potentially emetic drugs administered during longer procedures. Our results are consistent with the previously reported 17.5% incidence of PONV for anesthesia lasting 30-90 min, which increased to 46% for procedures lasting 150-210 min.[9]

The type of surgery was a significant predictor of PONV. Patients undergoing plastic, ophthalmologic, and orthopedic shoulder surgery were at least six times more likely to experience PONV than were patients in the reference group. Compared with the reference group, patients having ENT-dental, nonshoulder orthopedic, and non-D&C gynecologic surgery were two to four times as likely to experience PONV. ENT and dental surgery and orthopedic surgery involve bone injury and damage to the periosteum, resulting in significant postoperative pain. Similarly, recent studies support the high incidence of severe pain after plastic surgery.[26] There is evidence that nausea often accompanies pain in the early postoperative period and that both can be relieved in many cases by using intravenous opiates.[27] Further study of an improved effect of postoperative analgesia on the incidence of PONV in ENT and dental, orthopedic, and plastic surgery outpatients is needed.

Only 29.8% of the patients in this study were interviewed by telephone 24 h after discharge. The absence of an interpreter made language barriers difficult to overcome. Patients who had returned to work missed the daytime telephone calls. Furthermore, the sensitive nature of some surgical procedures, such as D&C, may have led to patient refusals.

A limitation of this study was the potential for underreporting of PONV by the PACU or ASU nurses. A heavy workload could decrease the amount of observed active patient retching. In addition, because of the large sample size within this study, small differences could reach be statistically significant yet clinically insignificant.

A history of motion sickness is associated with an increased incidence of PONV.[23] A large prospective survey of a wide spectrum of procedures concluded that a history of motion sickness was the fourth strongest predictor of PONV.[20] Ultimately, a previous history of motion sickness was not included in our analysis of the predictive factors of PONV.

Using an independent set of patients for validation, our model achieve fairly good prediction accuracy, yielding an area under the ROC curve of 0.785. This area is consistent with previously reported models.[22] The correlation between the median predicted probabilities and the observed frequencies of PONV in the 10 percentile risk groups was excellent ($r^2 = 0.99$, $P < 0.0001$). Statistical comparison of the predictive performance this model and the previously reported predictive models is warranted in a prospective study of one patient population to identify the best predictive model.

A well-designed logistic regression model of factors associated with PONV will help guide patient selection for antiemetic therapy. Palazzo and Evans[23] developed a model to predict PONV. However, their study has several limitations. Because the coefficients of the study were derived from a small sample of patients having orthopedic surgery, the model is not applicable to various types of surgical patients. The model also lacks validation by statistical techniques that evaluate the model's ability to predict PONV correctly. Koivuranta *et al.*[20] developed a risk score to predict PONV and measured the power of the model by calculating the area under the ROC. Although patient and surgery related factors were addressed in their model, the coefficients were derived from pediatric and adult inpatients. Anesthesia-related factors were not included. Similarly, The predictive model developed by Apfel *et al.*,[22] which was derived from adult inpatients, also lacks anesthesia-related factors. Unlike patient-related factors and many surgery-related factors that cannot be modified in the perioperative period, many anesthesia-related factors, such as anesthetic technique, sometimes can be modified. Anesthesia-related factors must be included in the model to determine the potential effect of a change in anesthetic technique. We present the only model that is derived from ambulatory patients and incorporates anesthesia-related factors. This model is the most comprehensive logistic regression model of patient-, anesthesia-, and surgery-related factors associated with PONV (see appendix 1). This model will be able to predict patients' risk for PONV according to their sex, age, previous PONV, history of motion sickness, duration of anesthesia, anesthetic technique, and type of surgery. We evaluate the model's ability to correctly predict PONV and determine the power of the model by calculating the area under the ROC curve.

Knowledge of these predictors of PONV should increase anesthesiologists' efforts to reduce the incidence of PONV by selecting patients for antiemetic therapy. This may lead to improved cost-effective use of available drugs and resources.

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Appendix 1

Logistic regression is used to model the relation between explanatory variables and binary outcome variables. The logistic regression modeling assumes that the probability of an event (*i.e.*, the occurrence of the outcome) is associated with the values of the explanatory variables in the following way:

$$p = 1/(1 + e^{-\mathrm{logit}(p)})$$

where

$$\mathrm{logit}(p) = \beta_0 + \beta_1 x_i + \ldots + \beta_n x_n$$

where p = probability of the occurrence of the outcome, x_i = value of the i^{th} independent variable, and β_i events for any patient = parameter estimates for the i^{th} variable.

Fitting the model to the data, we can obtain the maximum likelihood estimate of the parameters for each variable. Based on the maximum likelihood estimates from the final models, it is possible to calculate an expected risk of occurrence of the specific adverse event for any patient.

$$\begin{aligned}\mathrm{logit}(p) = {} & -5.97 + -0.14 \cdot \mathrm{Age} + -1.03 \cdot \mathrm{Sex} + \\ & -0.42 \cdot \mathrm{Smoke} + 1.14 \cdot \mathrm{PONVHistory} + 0.46 \cdot \mathrm{Duration} \\ & + 2.36 \cdot \mathrm{GA} + 1.48 \cdot \mathrm{ENT} + 1.77 \cdot \mathrm{Ophthalm} + 1.90 \cdot \mathrm{Plastic} \\ & + 1.20 \cdot \mathrm{GynNonDC} + 1.04 \cdot \mathrm{OrtKnee} + 1.78 \cdot \mathrm{OrtShoulder} \\ & + 0.94 \cdot \mathrm{OrtOther}\end{aligned}$$

where Age = age in years/10; Sex = 1 if male and 0 if female; Smoke = 1 if smoker and 0 if nonsmoker; PONV History = 1 if previous PONV and 0 if no previous PONV; Duration = duration of surgery in 30-min increments; GA = 1 if general anesthesia and 0 if other type of anesthesia; ENT = 1 if ENT and 0 if other type of surgery; Ophthalm = 1 if ophthalmology and 0 if other type of surgery; Plastic = 1 if plastic surgery and 0 if other type of surgery; GynNonDC = 1 if gynecologic non D&C procedure and 0 if other type of surgery; OrtKnee = 1 if orthopedic procedure involving knee and 0 if other type of surgery; OrtShoulder = 1 if orthopedic procedure involving the shoulder and 0 if other type of surgery; OrtOther = 1 if orthopedic procedure involving neither knee nor shoulder and 0 if other type of surgery.

Examples

The risk for patient 1, a 30-yr-old woman with a history of smoking and previous PONV undergoing a 1-h shoulder (orthopedic) operation with general anesthesia is 35.2%.

$$p = 1/(1 + e^{-(-5.97 + -0.14 \cdot 3 + -0.42 \cdot 1 + 1.14 \cdot 1 + 0.46 \cdot 2 + 2.36 * 1 + 1.78 * 1)}) - 0.352.$$

The risk for patient 2, a 40-yr-old nonsmoking man with no previous PONV undergoing a 1-h knee arthroscopy (orthopedic) without general anesthesia is 0.4%.

$$p = 1/(1 + e^{-(-5.97 + -0.14 \cdot 4 + -1.03 \cdot 1 + 0.46 \cdot 2 + 1.04 \cdot 1)}) = 0.004.$$

The risk for patient 3, a 70-yr-old smoking man with no previous PONV undergoing a 1-h cataract surgery (ophthalmologic) without general anesthesia is 0.3%.

$$p = 1/(1 + e^{-(-5.97 + -0.14 \cdot 7 + -1.03 \cdot 1 + -0.42 \cdot 1 + 0.46 \cdot 2 + 1.77 \cdot 1)}) = 0.003.$$

The risk for patient 4, a 32-yr-old nonsmoking woman with previous PONV undergoing a 30-min laparoscopy (gynecologic) with general anesthesia is 22.1%

$$p = 1/(1 + e^{-(-5.97 + -0.14 \cdot 3.2 + 1.14 \cdot 1 + 0.46 \cdot 1 + 2.36 \cdot 1 + 1.20 \cdot 1)}) = 0.221.$$

The risk for patient 5, a 22-yr-old woman with a history of smoking and previous PONV undergoing a 90-min bilateral breast augmentation (plastic surgery) with general anesthesia is 52%.

$$p = 1/(1 + e^{-(-5.97 + -0.14 \cdot 2.2 + -0.42 \cdot 1 + 1.14 \cdot 1 + 0.46 \cdot 3 + 2.36 \cdot 1 + 1.90 \cdot 1)}) = 0.520.$$