

A risk score-dependent antiemetic approach effectively reduces postoperative nausea and vomiting – a continuous quality improvement initiative

[Un traitement antiémétique relié au score de risque réduit efficacement les nausées et les vomissements postopératoires - une initiative d'amélioration continue de la qualité]

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Purpose: In a previous survey, patients at risk for postoperative nausea and vomiting (PONV) were best identified by a simplified risk score. Consequently, we investigated whether a risk score-dependent antiemetic strategy could effectively reduce the incidence of PONV in our department.

Methods: Adult in-patients ($n = 428$) scheduled for throat, thyroid, breast or gynecological surgery under general anesthesia were prospectively classified in three risk groups (L = low, M = medium, H = high) by using a simplified risk score. Patients in the L group did not receive any antiemetic prophylaxis. Patients in the M group received volatile anesthesia with 0.625 mg droperidol or an iv propofol anesthesia without droperidol. Patients in the H group received iv anesthesia supplemented with 4 mg dexamethasone and 0.625 mg droperidol.

Results: Compared with the data from our previous survey, the overall incidence of PONV decreased from 49.5% to 14.3% ($P < 0.001$). The incidence decreased from 34% to 13.2% ($P < 0.001$) in the M group and from 64.3% to 15.5% ($P < 0.001$) in the H group. Mean postanesthesia care unit time decreased from 99 to 82 min ($P < 0.04$).

Conclusion: This is the first survey which suggests that the departmental incidence of PONV can be significantly lowered by a risk score-dependent antiemetic strategy through a quality improvement initiative.

Objectif: Lors d'une enquête antérieure, des patients à risque d'avoir des nausées et des vomissements postopératoires (NVPO) ont été recensés par un score de risque simplifié. De là, nous voulions savoir si un traitement antiémétique relié au score de risque pouvait efficacement réduire l'incidence de NVPO.

Méthode : Des adultes hospitalisés ($n = 428$) pour une intervention chirurgicale pharyngienne, thyroïdienne, mammaire ou gynécologique sous anesthésie générale ont été répartis de façon prospective en trois groupes de risque (F = faible, M = modéré, E = élevé) en utilisant un score de risque simplifié. Les patients du groupe F n'ont pas reçu de traitement antiémétique préventif. Ceux du groupe M ont reçu une anesthésie volatil avec 0,625 mg de droperidol ou une anesthésie iv au propofol sans droperidol. Ceux du groupe E ont reçu une anesthésie iv complétée par 4 mg de dexaméthasone et 0,625 mg de droperidol.

Résultats : Comparés aux données obtenues de l'enquête, l'incidence totale de NVPO a chuté, passant de 49,5 % à 14,3 % ($P < 0,001$). L'incidence a baissé de 34 % à 13,2 % ($P < 0,001$) dans le groupe M et de 64,3 % à 15,5 % ($P < 0,001$) dans le groupe E. Le séjour moyen en salle de réveil a diminué de 99 à 82 min ($P < 0,04$).

Conclusion : C'est la première enquête qui montre que l'incidence de NVPO dans notre service peut être significativement réduite par un traitement relié au score de risque.

THE incidence of postoperative nausea and vomiting (PONV) is still in the range of 25 to 30%.¹ Avoiding PONV is one of the highest priorities for most patients and anesthesiologists.^{2,3} Nevertheless, non-selective antiemetic prophylaxis does not improve outcomes unless patients are at high risk for PONV.⁴ Recently, risk scores for predicting PONV have been proposed as a tool to classify patients according to their predicted risk and to apply prophylactic antiemetics based on

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this classification.^{5,6} For daily clinical purposes, simplified risk scores^{7,8} are easy to handle and show a good correlation between the expected and actual incidence of PONV in in-patients.⁹ In addition, the simplified risk score by Apfel *et al.* presented with favourable discriminating and calibration properties for predicting the risk of PONV in our hospital.¹⁰ Since our university-affiliated hospital is the primary cancer centre with a high proportion of female patients, the overall incidence of PONV was 49.5%.¹⁰ Thus, we sought to verify whether the application of a risk score-dependent antiemetic strategy can effectively reduce the overall incidence of PONV in our department.

Methods

After approval from our Institutional Ethics Committee and obtaining written informed consent from all subjects, we prospectively studied 548 consecutive surgical in-patients in the cancer referral hospital of Toulouse between January 18 and May 17, 2002. All patients were adults; American Society of Anesthesiologists physical status I to III; and scheduled for elective throat, thyroid, breast, or gynecological surgery under general anesthesia. Ten patients, who underwent a second surgical operation for hematoma within the first 24 hr, were excluded; 82 patients were excluded because of protocol violations; and 28 because they received preoperative antiemetic drugs. In order to gather data from the same number of patients as in our previous report,¹⁰ we stopped the study when we had useable data from 428 patients.

The simplified risk score was calculated preoperatively for each patient.⁷ This predictive score of PONV considers four predictors: female sex, history of PONV or motion sickness, non-smoking status, and the expected use of postoperative opioids; patients were assigned one point for each of the risk factors. In a cross-validation study, patients with a risk factor score of 0 had a 10% risk for PONV; those with a score of 1 had a risk of 21%; of 2, 39%; of 3, 61%; and of 4, 79%. Patients were then stratified according to their risk score to receive a prophylactic antiemetic regimen as follows: 1) low risk group (zero or one risk factor, predicted incidence of PONV \leq 21%): no prophylaxis; 2) medium risk group (two risk factors, predicted incidence of PONV = 39%): balanced anesthesia with 0.625 mg droperidol about 30 min before extubation or *iv* anesthesia with propofol for induction and maintenance at the discretion of the anesthesiologist; 3) high risk group (three or four risk factors, predicted incidence of PONV \geq 61%): *iv* anesthesia with propofol, supplemented with 4 mg dexamethasone after induction and 0.625 mg droperidol about 30 min before extubation.

The anesthetic regimen was similar to that described in our previous study.¹⁰ Ten milligrams midazolam or 0.5 mg alprazolam were given orally for premedication. Induction of anesthesia was performed with 10 to 15 μ g sufentanil and 2 to 3 $\text{mg}\cdot\text{kg}^{-1}$ propofol (more if clinically necessary). Intubation was facilitated with 0.15 $\text{mg}\cdot\text{kg}^{-1}$ cisatracurium or mivacurium. Anesthesia was maintained with volatile anesthetics (sevoflurane or desflurane) or propofol (7 to 8 $\text{mg}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$) according to the risk stratification, and 5 μ g boluses of sufentanil were given as dictated by clinical need. Neuromuscular blockade was reversed with neostigmine 40 $\mu\text{g}\cdot\text{kg}^{-1}$ and atropine 15 $\mu\text{g}\cdot\text{kg}^{-1}$ in four patients.

Postoperative analgesia was achieved with *iv* paracetamol, 2 g, and ketoprofene, 50 mg, four times per day; the first dose was given 45 min before the end of surgery. In the postanesthesia care unit (PACU), analgesia was provided with *iv* boluses of morphine 2 mg and repeated until the patients were comfortable. In the surgical unit, nalbuphine 20 mg was administered intravenously if analgesia, as assessed with a visual analogue scale (VAS), was inadequate (VAS \geq 40 mm).

Guidelines for rescue antiemetic were 1 mg ondansetron *iv* for the first and 0.625 mg droperidol intravenously for the second episode of PONV. If PONV persisted, the anesthesiologist was to consider hydroxyzine (25 mg *iv*).

In the PACU and in the surgical unit, trained nurses, blinded to the prophylactic antiemetic protocol, recorded any episodes of retching or vomiting. Nausea was assessed during the PACU stay and before the transfer to the ward and at two, six and 24 hr postoperatively. Nausea was evaluated on a three-point scale: 0 (no nausea), 1 (mild nausea), and 2 (severe nausea). A patient was classified as having PONV if any nausea, or vomiting occurred within the first 24 postoperative hours. On the following day, the two investigators (S.P. and G.C.) interviewed nurses, reviewed records and anesthetic protocol, and consulted patients to ensure high quality data collection. All patients stayed at least 24 hr in the surgical unit (in-patients).

Results from this survey were compared with those from our previous study, which validated the simplified risk score in our clinical setting.¹⁰ Data are presented as means and their confidence intervals (CI) for quantitative variables unless otherwise specified. Categorical factors are expressed as proportions. Differences in means and proportions were analyzed between the two studies with Chi square tests and Fisher's exact tests when appropriate. A post hoc power analysis revealed that the sample size of 428

patients in each survey had a power of 99% ($\beta = 0.01$) to detect a reduction of PONV from 50% to 25% in the second survey within the 95% CI limits ($\alpha = 0.05$).

Results

There were no significant differences between our study and the previous survey with regard to age, female sex, and non-smoking status (Table I). In the present study, the duration of anesthesia was significantly longer and more patients reported previous PONV or motion sickness, but fewer were expected to require postoperative opioids. As a result, the overall distribution of patients according to the simplified risk score was not significantly different from the previous survey.¹⁰ Most patients were non-smoking women without a previous history of PONV undergoing breast surgery.

The overall incidence of PONV for the zero to 24 postoperative hours decreased from 49.5% (95% CI = 0.44–0.54) in the previous survey¹⁰ to 14.3% (0.11–0.18) in this survey (Figure 1; $P < 0.001$). Similarly, the overall incidence of vomiting decreased from 25.9% (0.22–0.30) in the first survey¹⁰ to 6.8% (0.05–0.10) in the present survey ($P < 0.001$). Overall, 1.6% (0.07–3.3) of the patients in the current survey suffered PONV in the PACU and 8.9% (6.4–12) during the first six postoperative hours. In contrast, 18.7% (15–22.4) of the patients in the first survey¹⁰ experienced PONV in the PACU and 40.7% (36–45.3) during the first six postoperative hours.

The incidence of PONV in the subgroups with low (score of 0 or 1) risk factors in the two surveys was similar (Table II and Figure 2). On the other hand, the medium (score of 2) and high risk-factor (score of 3 or 4) subgroups in the current survey had significantly fewer episodes of PONV than previously (Table II and Figure 2). The prophylactic antiemetic strategy in our current survey reduced the incidence of PONV by approximately 50% in the medium risk group and 75% in the high-risk group (Figure 2).

In the medium risk group, where the anesthesiologist could choose between balanced anesthesia with droperidol and an *iv* approach with propofol, the incidence of PONV was similar with 14.5% (0.08–0.24) in-patients who received propofol ($n = 83$) and 12.1% (0.06–0.20, $P = 0.66$) in-patients who received droperidol ($n = 99$).

Discussion

Recent clinical guidelines suggest that the choice between prophylactic or rescue antiemetic treatment should depend on the patient's risk for PONV.¹¹ A previous recommendation suggested to classify

TABLE I Demographic data and patient distribution

	Previous survey ($n = 428$) ¹⁰	Current survey ($n = 428$)	<i>P</i> value
Age (yr)*	53 (35–71)	52 (35–69)	0.27
Female sex	386 (90)	394 (92)	0.34
Previous PONV or motion sickness	97 (23)	140 (33)	0.001
Smoking	102 (24)	88 (21)	0.25
Expected use of postoperative opioids	295 (69)	187 (44)	< 0.001
Duration of anesthesia # (min)	81 (76–85)	111 (103–119)	< 0.001
Type of surgery			0.013
Throat and thyroid surgery	105 (24)	75 (18)	
Breast surgery	290 (68)	301 (70)	
Gynecological surgery	33 (8)	52 (12)	
Time in PACU (min) #	99 (95–103)	82 (78–86)	0.04
Simplified risk score			0.08
0	4 (1)	5 (1)	
1	42 (10)	35 (8)	
2	144 (34)	182 (43)	
3	178 (42)	162 (38)	
4	60 (14)	44 (10)	

PACU = postanesthetic care unit; PONV = postoperative nausea and vomiting. *Results for age are given as medians (lower-upper quartiles); #For duration of anesthesia and time in PACU as means (95% confidence interval); and for all other variables as number of patients (% of total).

TABLE II Incidences of PONV according to the simplified risk score

	Previous survey ($n = 428$) ¹⁰	Current survey ($n = 428$)	<i>P</i> value
Simplified risk-score			
0 (0–0.60)	0 (0–0.60)	0 (0–0.52)	N/A
1	23.8 (0.12–0.39)	14.3 (0.05–0.30)	0.39
2	34 (0.26–0.42)	13.2 (0.08–0.18)	< 0.001
3	57.3 (0.50–0.65)	14.2 (0.09–0.20)	< 0.001
4	85 (0.73–0.93)	20.5 (0.10–0.35)	< 0.001

PONV = postoperative nausea and vomiting; N/A = not applicable. Results are given as percentage (95% confidence interval).

patients into one of four risk groups for PONV: low-risk (< 10%), mild-to-moderate risk (10–30%), high risk (30–60%) and very high risk (> 60%) of PONV.⁵ The classification is based on the number of risk factors patients have. We investigated whether a strategy based on scoring of risk could effectively reduce the incidence of PONV in our practice. Although such a risk factor-dependent prophylactic antiemetic strategy is intuitively convincing and straightforward, it has never been validated in clinical practice. To our knowl-

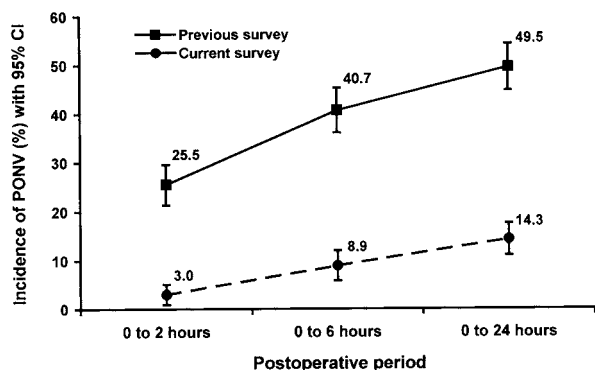


FIGURE 1 The incidence of postoperative nausea and vomiting (PONV) for the first two, six, and 24 postoperative hours in the current and previous¹⁰ surveys. The two groups were significantly different from one another at every time interval; $P < 0.001$. CI = confidence intervals.

edge, this is the first clinical trial showing that, in comparison with historical data, a risk score-dependent prophylactic antiemetic strategy decreased the overall institutional rate of PONV from 49.5% to 14.3% and shortened the PACU stay.

The patients in our current survey received anesthetic and antiemetic treatment according to protocol. It is generally accepted that patients with a low risk for PONV do not benefit from prophylactic antiemetic treatment and, therefore, patients with a risk factor score of 0 or 1 received a standard anesthetic. Inpatients with moderate risk, there is no generally accepted anesthesia standard, but data from a recent study strongly suggest that volatile anesthetics appear to be the major cause for early postoperative vomiting.¹² Therefore, we favoured a propofol-based *iv* anesthetic in this group of patients. However, anesthesiologists who preferred to use an inhalational anesthetic were asked to give an antiemetic, i.e., 0.625 mg droperidol 30 min before the end of the case. Droperidol was used instead of ondansetron for economical reasons, and because ondansetron is ineffective for the treatment of established PONV when it has already been given prophylactically.¹³ Our high-risk patients received total *iv* anesthesia supplemented with dexamethasone and droperidol. When a patient's risk for PONV is high, a single antiemetic strategy is insufficient and a multimodal approach is necessary.¹⁴ Which antiemetics, alone or in combination, should be used when a propofol-based *iv* anesthetic is used is unknown; therefore, we decided to supplement the *iv* anesthesia with 4 mg dexamethasone (minimally effective

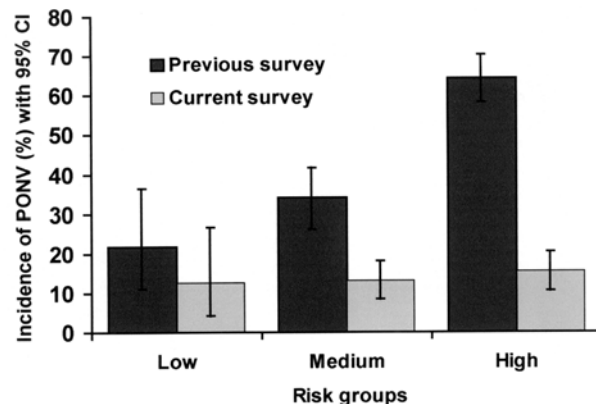


FIGURE 2 The incidence of postoperative nausea and vomiting (PONV) in the first 24 postoperative hours graphed according to risk group classification in the current and previous¹⁰ surveys. Low = a risk score of 0 or 1; medium = a risk score of 2; and high = a risk score of 3 or 4. CI = confidence intervals.

tive dose 2.5 to 5 mg¹⁵ given at the beginning of the case)¹⁶ and 0.625 mg droperidol given 30 min before the end of the case.¹⁷ We chose not to add metoclopramide since, despite its well-established use in PONV, a recent meta-analysis showed that it is not an effective antiemetic.¹⁸

The 35.2% absolute risk reduction of the 24-hr incidence of PONV was similar to that obtained with a systematic multimodal antiemetic prevention in an outpatient population undergoing gynecological laparoscopic surgery;¹⁴ however, the multimodal approach may be more expensive since every patient receives both propofol and antiemetics. The number needed-to-treat (NNT) with propofol and droperidol is around 5,¹⁷ which corresponds to our results in the medium-risk group (NNT = 4.8). In the high-risk group, two patients need to be treated with propofol based *iv* anesthesia supplemented with dexamethasone and droperidol to prevent PONV in one patient, which is similar to the findings observed with a droperidol, dexamethasone, ondansetron, and metoclopramide combination.¹⁹

A randomized controlled trial is the gold standard by which treatment effect is measured. Under narrowly defined conditions, a treatment effect that leads to valid results for the investigated population can be quantified precisely. Such studies reveal that, in order to reduce PONV, propofol needs to be given not only for induction but also for maintenance;²⁰ droperidol is sufficient when given at the end of anesthesia, and 2.5 to 5 mg dexamethasone should be given at the beginning rather than the end of anesthesia.¹⁶ Additionally, a combina-

tion of antiemetics (multimodal approach) is superior to a single antiemetic.¹⁴ Therefore, the above-mentioned risk-dependent antiemetic strategy as suggested by White and Watcha appears sound.^{5,6} In order to put such a system into practice, our quality assurance team decided to approach this problem in two steps:

1) The extent of the problem needed to be quantified by determining the incidence of PONV in our institution. In addition, if a risk-score dependent antiemetic strategy was to be established, evidence was needed that a risk score can identify the patients at risk for PONV in our department.

2) If a patient's risk is predictable, an antiemetic strategy ought to demonstrate that the incidence of PONV can be significantly lowered in a second survey.

To satisfy the first step, we determined in our initial survey that the overall incidence of PONV is 49.5%, and found that the simplified risk score by Apfel *et al.*⁹ provides a good risk prediction for our department.

For the second step we decided to investigate, in this quality assurance initiative, whether the described risk-score dependent antiemetic strategy leads to a reduced incidence of PONV. Theoretically, this should have been investigated in a randomized controlled trial - but at the expense that half of the patients at increased risk would be denied effective antiemetic treatment. In the light of the plethora of randomized controlled trials, which have shown that antiemetics are effective, we felt that, in accordance with Aspinall and Goodman, such a study design was ethically questionable.²¹ Therefore, we chose to apply this risk-score dependent antiemetic approach to a subsequent 428 patients, being aware that a more cautious interpretation was needed because the 'level of evidence' of a survey is lower than that of a randomized controlled trial.

The critical point with our approach is the issue of group comparability. While age, female sex, and the non-smoking status were similar, other risk factors were not. For example, the previous survey may have led to an increased awareness that postoperative opioids cause PONV and may, therefore, have led to a decreased use of opioids in the present survey. This could have lowered the incidence of PONV independently from the predetermined treatment strategy. On the other hand, the duration of surgery was increased (probably because of some new younger surgeons) and this may have increased the incidence of PONV despite the fact that this risk factor is weaker.⁸ As shown in Table I, the type of surgery was different. Since several recent studies in in-patients suggest that the type of surgery has little impact on PONV⁷⁻⁹ and - even more importantly - had no impact in our previ-

ous survey,¹⁰ it is very unlikely that these small differences confounded the results. Additionally, in our current survey there were more patients with a history of motion sickness or PONV, which would tend to decrease the effectiveness of our interventions. Overall, when the four most important risk factors are considered in the calculation of the risk score, the risk between the two surveys was similar. Thus, even if the average risk for PONV was slightly lower in our current population, it is very unlikely that the extreme reduction from 49.5% in the previous study to 14.3% happened by chance ($P < 0.001$). This is corroborated by risk-adjusted comparisons. In addition, in our low-risk group where no antiemetic intervention was performed, the incidence did not differ significantly from our previous survey ($\leq 21\%$). Thus, the overall reduction of PONV from 49.5% to 14.3% results from a reduced incidence in the medium- and high-risk groups that received an intervention.

In conclusion, the data from this survey suggest that the use of a simplified risk score-dependent prophylactic antiemetic strategy can significantly reduce the overall institutional rate of PONV and shorten stay in the PACU.

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