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Evidence-based analysis of risk factors for postoperative nausea and vomiting†

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Editor's key points

- Identifying independent predictors for postoperative nausea and vomiting (PONV) would be useful.
- Systematic review of 22 large (>500 patients each) studies identifying predictors of PONV.
- Female, previous PONV, non-smoker, younger age, volatile anaesthetics, and postoperative opioids were predictors.
- Some factors commonly thought to be predictors were not.

Background. In assessing a patient's risk for postoperative nausea and vomiting (PONV), it is important to know which risk factors are independent predictors, and which factors are not relevant for predicting PONV.

Methods. We conducted a systematic review of prospective studies ($n>500$ patients) that applied multivariate logistic regression analyses to identify independent predictors of PONV. Odds ratios (ORs) of individual studies were pooled to calculate a more accurate overall point estimate for each predictor.

Results. We identified 22 studies ($n=95\,154$). Female gender was the strongest patient-specific predictor (OR 2.57, 95% confidence interval 2.32–2.84), followed by the history of PONV/motion sickness (2.09, 1.90–2.29), non-smoking status (1.82, 1.68–1.98), history of motion sickness (1.77, 1.55–2.04), and age (0.88 per decade, 0.84–0.92). The use of volatile anaesthetics was the strongest anaesthesia-related predictor (1.82, 1.56–2.13), followed by the duration of anaesthesia (1.46 h^{-1}, 1.30–1.63), postoperative opioid use (1.39, 1.20–1.60), and nitrous oxide (1.45, 1.06–1.98). Evidence for the effect of type of surgery is conflicting as reference groups differed widely and funnel plots suggested significant publication bias. Evidence for other potential risk factors was insufficient (e.g. preoperative fasting) or negative (e.g. menstrual cycle).

Conclusions. The most reliable independent predictors of PONV were female gender, history of PONV or motion sickness, non-smoker, younger age, duration of anaesthesia with volatile anaesthetics, and postoperative opioids. There is no or insufficient evidence for a number of commonly held factors, such as preoperative fasting, menstrual cycle, and surgery type, and using these factors may be counterproductive in assessing a patient's risk for PONV.

Keywords: PONV; risk; vomiting, nausea, anaesthetic factors; vomiting, nausea, patient factors; vomiting, nausea, surgical factors

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Postoperative nausea and/or vomiting (PONV) is an unpleasant experience that afflicts 20–30% of surgical patients after general anaesthesia.[1] PONV decreases patient comfort and satisfaction, and, rarely, may cause dehydration and electrolyte imbalances, aspiration of gastric contents, oesophageal rupture, suture dehiscence, and bleeding.[2–9] PONV and its resulting complications are costly for the healthcare sector worldwide, with several hundred million dollars spent annually in the USA alone.[10]

PONV is a multifactorial phenomenon that can be triggered by multiple receptor pathways at peripheral, central, or both sites.[11] A number of patient-specific, anaesthesia-related,

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and surgery-related risk factors have been associated with higher incidences of PONV. Although risk factors have merely a correlative relationship with a given outcome, they can nevertheless be clinically useful. In contrast, independent predictors are more likely to have a causative relationship, and they may be used to predict or explain an outcome when statistically corrected for other factors or confounders. Over the past few years, several groups have used multivariate logistic regression analyses to pinpoint which risk factors for PONV are independent predictors. In some cases, scores based on these independent predictors were developed, and in general, the attention paid to PONV has greatly improved in clinical practice.[2 4 5 12–14]

While general reviews on PONV, including one review dedicated to risk factors,[11] reflect authors' opinions, there has been no systematic, evidence-based review that attempts to quantify the relative impact of independent predictors for PONV. Therefore, we conducted a systematic literature search and synthesized the data on all proposed risk factors of PONV to calculate accurate overall point estimates for each. The primary emphasis of this analysis is on quantification, not identification, in order to establish which patient-specific, anaesthesia-related, and surgery-related risk factors are indeed independent—and thus potentially causal—predictors.

Methods

Systematic identification of all available evidence

To identify all available evidence, we systematically searched the databases of PubMed, EMBASE, and Cochrane with no restrictions on publication date, language, or status. The search was performed by two investigators (F.M.H., K.Z.) and verified by another (C.C.A.). The last systematic electronic search was performed in November 2011. The following four-legged search string consisting of free text phrases and medical subject heading (MeSH) indexing terms: '(postoperative or post-operative or Surgical Procedures, Operative[mh] or anesthesia or anaesthesia or postanesth* or postanaesth* or post-anesth* or post-anaesth* or surgery or surgical or surgeries) and (nausea or vomit* or emesis or retching or Postoperative Nausea And Vomiting[mh]) and (risk factor or Risk Factors[mh] or predictor) and (logistic or regression or model or Risk Assessment/methods[mh] OR Logistic Models[mh] OR Discriminant Analysis[mh]).'

To identify additional potentially relevant data sources, we hand-searched the reference lists of the retrieved studies and the databases of major related journals, including *Anaesthesia, Anesthesiology, British Journal of Anaesthesia (BJA), British Medical Journal (BMJ), Journal of the American Medical Association (JAMA)*, and the *New England Journal of Medicine (NEJM)*. Finally, experts in the field were consulted until no additional potentially relevant source of data could be identified.

Inclusion criteria

All retrieved studies were systematically evaluated and reviewed by three independent investigators (F.M.H., K.Z., C.C.A.) for inclusion in the meta-analysis. We included randomized controlled trials (RCTs) and large epidemiological observational studies that enrolled at least 500 adult patients (age $\geq$15 yr old) and that identified independent predictors of PONV by means of multivariate logistic regression analysis. We included only studies in $>$500 patients because large studies provide the most reliable data with a high level of evidence, which is in contrast to studies with small sample sizes that can lead to randomly high (or low) point estimates. Because of the many assumptions that are needed for multivariable analyses, there is no accurate standard formula for sample size estimations available, but we agreed that a sample size of 500 would provide a reasonable threshold. Duplicate data, that is, studies reporting the same data in more than one publication, were excluded and only the data published in the primary article were included in the analysis. For inclusion, studies had to report adjusted odds ratios (ORs) [including the corresponding 95% confidence intervals (CI)] or respective regression coefficients [including the corresponding standard errors (SE)] for the occurrence of postoperative nausea (PN), vomiting (PV), or both (PONV). The studies were also required to meet the highest level of evidence. As the patients could not have been randomized by their risk of PONV, evaluation of these prognostic studies required the use of a different scale than that for evaluating RCTs. We included studies that met level II evidence according to the Oxford Centre for Evidence-Based Medicine guidelines,[15] where level I evidence is a systematic review of level II evidence, and level II evidence includes cross-sectional studies with consistently applied reference standards and blinding. No studies with inconsistently applied reference standards (level III), case–control studies (level IV), or mechanism-based reasoning pieces (level V) were included.

Nausea was defined as any unpleasant sensation with awareness of the urge to vomit. Vomiting was defined as successful or unsuccessful (retching) expulsion of gastric contents. PONV was defined as any nausea, vomiting, or both.

Data extraction

Data were extracted by one author (F.M.H.) and subsequently validated by a second independent investigator (K.Z.). All data were extracted as reported in the original article or as provided in supplementary material. In the case of missing data, the attempt was made to retrieve these data by contacting the corresponding author by e-mail. From each article, study design, year, country, number of centres, study endpoints and respective overall occurrence, number of study participants, all reported independent risk factors of PN, PV, or PONV, adjusted ORs (and corresponding 95% CI) or regression coefficients (and corresponding SE) for all independent patient-specific, anaesthesia-related, and surgery-related predictors were recorded.

Statistical analysis

Review Manager (Version 5, The Cochrane Collaboration) was used to perform statistical analyses. Because only a few patients will vomit without experiencing nausea,