BJA Advance Access published June 6, 2014

British Journal of Anaesthesia Page 1 of 8
doi:10.1093/bja/aeu150

BJA

Risk factors for obstetric morbidity in patients with uterine atony undergoing Caesarean delivery†

A. J. Butwick[1]*, B. Carvalho[1] and Y. Y. El-Sayed[2]

[1] Department of Anaesthesia and [2] Department of Obstetrics and Gynaecology, Stanford University School of Medicine, Stanford, CA, USA

* Corresponding author. E-mail: ajbut@stanford.edu

Editor's key points

- Risk factors for haemorrhage-related morbidity among women undergoing Caesarean delivery who develop refractory uterine atony are uncertain.
- This retrospective study investigated these risk factors exploring a large US-based database.
- Identified risks were African-American race, Hispanic ethnicity, multiple gestation, placenta praevia, general anaesthesia and ASA class III or IV.

Background. Uterine atony (UA) is recognized as a leading cause of postpartum haemorrhage. However, knowledge of risk factors of haemorrhage-related morbidity among patients diagnosed with UA is uncertain. We investigated risk factors for haemorrhage-related morbidity among patients undergoing Caesarean delivery with UA.

Methods. We conducted a secondary analysis of data sourced from a 4-yr observational study at 19 US academic centres. Patients with UA were identified based on receiving methylergonovine or carboprost. Our primary outcome (haemorrhage-related morbidity) included a composite of intra- or postpartum transfusion; Caesarean hysterectomy; uterine or hypogastric artery ligation; intensive care admission for: pulmonary oedema, coagulopathy, adult respiratory distress syndrome, postoperative ventilation, or invasive line monitoring.

Results. Among 57 182 patients who underwent Caesarean delivery, 2294 (4%) patients developed UA. Haemorrhage-related morbidity occurred in 450 (19.6%) patients with UA. The risk of haemorrhage-related morbidity was increased among African-Americans [adjusted odds ratio (aOR)=2.36; 95% confidence interval (CI)=1.73–3.23], Hispanics (aOR=1.4; 95% CI=1.04–1.9), women with multiple gestations (aOR=1.59; 95% CI=1.06–2.38), placenta praevia (aOR=4.89; 95% CI=3.04–7.87), patients with ASA class III (aOR=1.4; 95 CI=1.03–1.9), or ASA class IV (aOR=5.88; 95% CI=2.48–13.9), exposure to general anaesthesia (GA) (aOR=2.4; 95% CI=1.59–3.62) and combined general and regional anaesthesia (aOR=4.0; 95% CI=2.62–6.09), and ≥2 prior Caesarean deliveries (aOR=1.62; 95% CI=1.1–2.39).

Conclusions. Among patients with UA undergoing Caesarean delivery, the risk of haemorrhage-related morbidity is increased in African-Americans, Hispanics, patients with multiple gestations, placenta praevia, ASA class III or IV, ≥2 prior Caesarean deliveries and those undergoing GA.

Keywords: Caesarean section; morbidity; uterine atony

Accepted for publication: 16 January 2014

Patients undergoing Caesarean delivery are known to be at increased risk of postpartum haemorrhage (PPH) compared with patients undergoing vaginal delivery.[1–3] As rates of Caesarean delivery in the USA have steadily increased (from 20.7% in 1996 to 32.8% in 2010),[4] it is speculated that the increasing Caesarean delivery rate has contributed to increase in the rate of PPH.[5]

Uterine atony (UA) is recognized as the leading cause of PPH.[5–8] During Caesarean delivery, pharmacological prophylaxis with uterotonic agents and manual measures (such as uterine massage) is routinely performed to initiate adequate uterine tone and reduce the risk of severe PPH. Despite the incorporation of these prophylactic measures into routine clinical practice, refractory UA may occur during Caesarean delivery requiring the use of second-line uterotonics (such as methylergonovine or carboprost) and other surgical or medical interventions (such as haemostatic brace suturing, interventional radiology, or hysterectomy).[9 10] In the setting of refractory UA, women can experience major postpartum bleeding and are at increased risk of severe haemorrhage-related morbidity resulting from profound anaemia, organ hypoperfusion, and complications resulting from invasive medical or surgical intervention for haemorrhage control.[11–14]

Risk factors for haemorrhage-related morbidity among women who develop refractory UA are uncertain. Identifying specific risk factors for severe haemorrhage-related morbidity may assist obstetricians and anaesthetists in using tailored

†This paper was presented, in part, as a poster at the 45th Annual Meeting of the Society for Obstetric Anesthesia and Perinatology, Puerto Rico, USA (April 24–28, 2013).

interventions and care strategies when managing patients with refractory UA. The primary aim of this study was to investigate patient characteristic, obstetric, anaesthetic, and intrapartum risk factors for severe haemorrhage-related morbidity among women who experience UA during Caesarean delivery.

Methods

Study design and data sources

We performed a secondary analysis of data (Caesarean Registry) sourced from a 4-yr observational study conducted by the Eunice Kennedy Shriver National Institute of Child Health and Development Maternal-Fetal Medicine Units (MFMU) Network. Conducted between January 1, 1999 and December 31, 2002 at 19 US academic centres, this study investigated the risk of uterine rupture in women with a prior Caesarean delivery undergoing a trial of labour compared with elective repeat Caesarean delivery; full details of the methodology and study design have been presented previously.[15] This study was exempt from Stanford University institutional review board approval as the Caesarean Registry data set contains de-identified data.

Within the Caesarean Registry, we identified 57 182 patients who underwent Caesarean delivery. We excluded 13 259 patients who had a vaginal birth after prior Caesarean delivery. We defined UA using an approach described in a previous study of UA employing data from the Caesarean Registry.[16] UA was determined by: (i) a recorded entry indicating a clinical diagnosis of UA (recorded as a dichotomous variable) and (ii) administration of a second-line uterotonic drug: methylergonovine (methergine), carboprost (hemabate), or both drugs in combination. Figure 1 shows the process of selection for our study population. All participating centres within the MFMU network use oxytocin infusion for atony prophylaxis. Although patient-level data on prophylactic oxytocin dosing regimens were not collected, standard prophylactic oxytocin regimens have been described for a number of designated obstetric centres: nine centres used oxytocin concentration=20 U litre^{-1} (range=125–250 ml h^{-1}), three centres used 40 U litre^{-1}, and one centre used 10 U litre^{-1}.[16]

We selected surgical procedures and complications that indicated haemorrhage-related morbidity or that occurred as a consequence of haemorrhage-related morbidity. This conceptual approach has been previously described in studies examining indicators of severe maternal morbidity during delivery hospitalizations.[12 17] In order to determine indicators for haemorrhage-related morbidity, we reviewed morbidity studies that included PPH and transfusion as indicators of severe maternal morbidity[12 14 17] and population-wide studies of PPH that used blood transfusion and procedures to control bleeding to identify women with severe pregnancy-related morbidity.[8 18] Indicators for haemorrhage-related morbidity were then determined based on availability of data within the Caesarean Registry. For our primary outcome, we applied a composite measure for haemorrhage-related morbidity, defined by the presence of any of the following: intraoperative or postpartum red blood cell transfusion; Caesarean hysterectomy; uterine artery ligation; hypogastric artery ligation; or intensive care unit (ICU) admission for at least one of the following criteria: pulmonary oedema, coagulopathy, adult respiratory distress syndrome, postoperative ventilation, presence of an arterial line or central line. The criteria selected for ICU admission were based on studies that have described interventions or complications linked to haemorrhage or transfusion related complications.[19] Total estimated blood loss was not reported in the Caesarean Registry.

We selected candidate variables as potential risk factors for haemorrhage-related morbidity. Candidate variables included: maternal age, race/ethnicity, BMI, gestational age at the time of delivery, singleton/multiple gestation, pre-existing diabetes mellitus, hypertensive disorders of pregnancy, chorioamnionitis, placental abruption, placenta praevia, number of prior Caesarean deliveries, presence of labour or attempted induction, ASA class, and mode of anaesthesia for Caesarean delivery. In the Caesarean Registry, obstetric patients were coded as ASA class II, III, or IV only. Using World Health Organization (WHO) classification for BMI class,[20] women were grouped into five categories of BMI using height and weight data taken at or within 2 weeks of delivery: normal weight or underweight (<25), overweight (25–29.9), obese class I (30–34.9), obese class II (35–39.9), and obese class III (40 or more). Induction was defined by the presence of any of the following methods: artificial rupture of membranes, cervidil, foley bulb, laminaria, misoprostol, oxytocin, or prostaglandin gel. We classified modes of anaesthesia into five categories: general and regional (spinal or epidural) anaesthesia, general without regional anaesthesia, spinal anaesthesia, epidural anaesthesia, and spinal plus epidural anaesthesia.

Statistical analysis

Univariate analyses were performed using the χ^2 test for categorical data to assess the associations between candidate variables and the composite outcome. Candidate variables that were associated with the composite outcome on univariate analysis ($P \leq 0.2$) were included as potential covariates in the initial multiple logistic regression model. We used variance inflation factor testing to identify collinearity between independent variables. In order to minimize inequality in numbers within BMI categories and to more clearly elucidate whether an increase in risk occurs with a change in BMI category, we also constructed quintiles for BMI (<27.06, 27.06–29.97, 29.98–33.04, 33.05–37.7, >37.7).

Step-wise backward elimination was performed to construct the parsimonious final model; $P<0.05$ was required for a variable to be retained in the multivariate model. We constructed separate multivariate models for BMI classes using the WHO criteria and quintiles. Model goodness of fit was evaluated using the Hosmer–Lemoshow statistic. We calculated the area under the receiver-operating characteristic curve (AUCROC) using standard methods to assess the predictive performance of each model.

For internal validation of each model, we used a 10-fold cross-validation procedure that used the full data set for