What's New in Obstetric Anesthesia: The 2014 Gerard W. Ostheimer Lecture

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The aim of this review is to synthesize key concepts and novel research from the published literature in obstetric anesthesia, obstetric practice, and maternal and perinatal health for the calendar year 2013. These topics were recently addressed in the "What's New in Obstetric Anesthesia" lecture presented at the 46th Annual Society of Obstetric Anesthesia & Perinatology Meeting in Toronto, Ontario, Canada. This lectureship, which began in 1975, was renamed in 1995 in honor of Dr. Gerald Ostheimer, a master clinician and researcher in the field. Articles were chosen based on their potential to impact future practice and investigation, to highlight obstetric anesthesiologists' role as peridelivery physicians, and to improve multidisciplinary coordination of care. The review begins with an assessment of the major threats to maternal and fetal safety and well-being, and the anesthesiologist's role in mitigating them. Current concepts in labor analgesia and intra- and postoperative cesarean delivery anesthesia/analgesia are explored. An annotated bibliography is included as Supplemental Digital Content (http://links.lww.com/AA/B86).

MATERNAL OUTCOMES

Historically, the U.K. Centre for Maternal and Child Enquiries provided in-depth analyses of maternal deaths from nationally maintained, clinically detailed databases. Using similar methodology, in 2013 a multidisciplinary group of perinatal experts published their analysis of 660 maternal deaths in France, occurring between the years 1998 and 2007.[1] Despite an increase in risk factors, such as advanced maternal age, obesity, and cesarean delivery, the reported maternal mortality ratio was stable over the time period, at 8 per 100,000 live births. The "direct" (i.e., pregnancy-related) causes of death were similar to those in the United Kingdom and United States and included hemorrhage (18%), hypertensive disorders of pregnancy (10%), amniotic fluid embolus and thromboembolism (each 10%–12%), early pregnancy death (5.1%), and sepsis (3.0%). Anesthesia-related deaths accounted for 1.8% of the "direct" deaths. Cardiovascular disease was the primary "indirect" cause of maternal death. Over half of the maternal deaths were judged to be potentially avoidable, often due to delay in or inadequate care delivered by obstetric and anesthesia providers. This deficiency was previously reported in several other high-income countries.[2–6]

In the United States, investigation of severe maternal morbidity and mortality is increasingly accomplished through analyses of large administrative datasets, particularly in the case of rare events.[7,8] Using the Medicaid Analytic eXtract dataset (years 2000 to 2007) and a cross validation technique, Bateman et al.[9] devised a simple measure to summarize the burden of illness in the obstetric population. This obstetric risk score, which performed better in the obstetric population than previously developed non-obstetric indices, has applications in epidemiologic, health services and comparative effectiveness research. The odds of maternal end-organ injury or death increased for each point increase in the comorbidity risk score (odds ratio [OR], 1.37; 95% confidence interval [CI], 1.35–1.39).

Obstetric Hemorrhage

Obstetric hemorrhage is the primary cause of maternal death worldwide. A 2013 retrospective review of the Nationwide Inpatient Sample, the largest U.S. inpatient health care utilization dataset representing approximately 20% of all delivery admissions, reported a doubling of the postpartum hemorrhage (PPH) rate (from 1.9 per 1000 deliveries in 1999 to 4.2 per 1000 deliveries in 2008, P value for yearly trend < 0. 0001), with increases in both severe atonic and nonatonic hemorrhage.[10] Many of the expected risk factors were present in the affected patients, including advanced maternal age (adjusted OR [aOR], 1.5; 95% CI, 1.5–1.6), multiple pregnancy (aOR, 2.8; 95% CI, 2.6–3.0), uterine fibroids (aOR, 2.0; 95% CI, 1.8–2.2), preeclampsia (aOR, 3.1; 95% CI, 2.9–3.3), chorioamnionitis (aOR, 2.9; 95% CI, 2.5–3.4), placenta previa or abruption (aOR, 7.0; 95% CI, 6.6–7.3), cervical laceration (aOR, 94.0; 95% CI, 87.3–101.2), uterine rupture (aOR, 11.6; 95% CI, 9.7–13.8), instrumented vaginal delivery (aOR, 1.5; 95% CI, 1.4–1.6), and cesarean delivery (aOR, 1.4; 95% CI, 1.3–1.5). However, changes in these risk factors explained only 5.6% of the PPH increase. This administrative dataset lacked the clinical detail necessary to explore other potentially relevant changes in maternal status (e.g., obesity) and obstetric practice (e.g., induction or augmentation of labor).

To address the hazards of PPH, obstetric hemorrhage treatment protocols have been developed by multidisciplinary teams around the world. The "New WHO Recommendations on Prevention and Treatment of Postpartum Hemorrhage" were released, outlining the strategic approach in low-income countries.[11] Uterotonic drugs, ideally oxytocin, should be used during the third stage of labor, and for intractable PPH. Temporizing measures, including bimanual uterine compression, nonpneumatic antishock garments, and external aortic compression, are indicated until further care is available.[11] The European Society of Anaesthesiology's expert "Guidelines for the Management of Severe Perioperative Bleeding" in obstetric hemorrhage emphasizess the importance of initiating uterotonic therapy, but progressing to mechanical uterine preservation maneuvers (i.e., B-Lynch or compression sutures

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or interventional radiologic techniques), with escalation to hysterectomy, if needed and feasible.[12] The guidelines stressed the use of plasma fibrinogen concentration to predict impending PPH, specifically serum values <2.9 g/L in the setting of a platelet count of 100×10^9 L^{-1} or less at labor onset, or <2 g/L in a parturient with bleeding, and multidisciplinary planning for known cases of placenta accreta. Data are lacking to guide specific transfusion triggers or hemoglobin concentration targets for acute resuscitation during PPH. However, these experts recommended balanced replacement with red blood cells, fresh frozen plasma, platelet concentrates, and cryoprecipitate, noting that baseline serum fibrinogen concentrations in pregnancy are higher than in the nonpregnant state. Tranexamic acid use should be considered (e.g., for obstetric bleeding, to reduce the duration of bleeding and transfusion needs), although small studies have been unable to assess thrombotic complications and mortality.[13] The ongoing international WOMAN (World Maternal Antifibrinolytic) double-blind randomized control trial (RCT) of tranexamic acid administration early in PPH, and its effect on reducing maternal mortality, hysterectomy, and other negative outcomes, will provide more definitive guidance in the future.[14] Finally, the successful use of cell salvage techniques was reflected in the guidelines and other 2013 reports, although a single case of hemodynamic collapse in a critically ill patient was described.[12,15,16]

A hemorrhage management checklist was among the 12 surgical-crisis checklists that Arriaga et al.[17] hypothesized would significantly improve adherence to best practices in crisis situations. Key steps in this checklist were requests for help, resuscitation with IV fluids, blood bank notification within 5 minutes of unexpected significant blood loss, and further resuscitation with blood products within the next 5 minutes. Chest compressions should be initiated within 1 minute of onset of ventricular fibrillation. In their RCT of simulated crises with 17 multidisciplinary operating room teams at 3 institutions, these investigators found that using the hemorrhage and other checklists protected against failure to adhere to critical steps (adjusted relative risk [aRR], 0.28; 95% CI, 0.18–0.42; $P < 0.001$). Ninety-seven percent of participants reported that they desired checklists in real-life events.

Hypertensive Disorders of Pregnancy/Preeclampsia

Hypertensive disorders of pregnancy were a prominent topic in 2013, featured in high-quality publications in >20 journals. The American College of Obstetricians and Gynecologists (ACOG) Task Force on Hypertension in Pregnancy published a critical review of the literature. Despite productive research in the field, there are still no clinically applicable tests that can be used early in pregnancy to reliably predict the impending development of preeclampsia.[18] Given the 25% increase in preeclampsia over the past 2 decades, with its associated considerable morbidity and mortality, the 2002 definition of preeclampsia was modified to promote early recognition and more standardized management of the disease (Table 1).[19] Proteinuria was removed as an absolute requirement to avoid delay in preeclampsia diagnosis. The term "mild preeclampsia" was replaced with "preeclampsia without severe features" to reflect the dynamic nature of the disease.

A high level of oversight and available resources to treat these mothers and their developing fetuses was deemed imperative. Serial maternal and fetal testing was recommended for women with gestational hypertension or preeclampsia without severe features. Delivery at 37 0/7 weeks' gestational age was recommended for women with preeclampsia without severe features. In stable patients with severe preeclampsia at <34 0/7 weeks' gestational age, pregnancy should be continued "only at facilities with adequate maternal and neonatal intensive care resources."

The active ante-, intra- and postpartum management of severe hypertension (i.e., blood pressure ≥160/110 mm Hg) was strongly advocated by the ACOG Task Force, as substandard treatment of high maternal blood pressure in patients with hypertensive disorders of pregnancy has been implicated in many of the 14% of maternal deaths related to stroke.[20] A 2013 Cochrane meta-analysis concluded that there is no superior antihypertensive drug; therefore, medication choice should be based on the clinician's familiarity and experience.[21] Nimodipine, diazoxide, ketanserin and magnesium sulfate (as an antihypertensive agent) are best

Table 1. Diagnostic Criteria for Preeclampsia

High blood pressure[a] • ≥140 mm Hg systolic or ≥90 mm Hg diastolic on 2 occasions at least 4 hours apart after 20 weeks' gestational age if previously normal blood pressure • ≥160 mm Hg systolic or ≥110 mm Hg diastolic, confirmed within a short interval	*and*	Proteinuria • ≥300 mg per 24-hour urine collection (or equivalent from a timed collection) *or* • Protein/creatinine ratio ≥0.3 (mg/dL) *or* • Dipstick reading of 1+ (only if other quantitative methods unavailable)
or		
New onset high blood pressure[a] • ≥140 mm Hg systolic or ≥90 mm Hg diastolic on 2 occasions at least 4 hours apart after 20 weeks' gestational age • ≥160 mm Hg systolic or ≥110 mm Hg diastolic, confirmed within a short interval	*and*	*New onset* of any of the following severe features: Thrombocytopenia • Platelet count <100,000/μL Renal insufficiency • Serum creatinine >1.1 mg/dL *or* • Doubling serum creatinine concentration in the absence of other renal disease Impaired liver function • Doubling normal blood concentrations of liver transaminases *and/or* • Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not due to an alternative diagnosis Pulmonary edema Cerebral or visual symptoms

[a]Severe features of preeclampsia are defined as having any ≥160 mm Hg systolic or ≥110 mm Hg diastolic or any of the other findings listed.
Source: American College of Obstetricians and Gynecologists Task Force on Hypertension.[19]

avoided. In an acute hypertensive emergency, oral nifedipine achieved target blood pressure more quickly than IV labetalol or placebo (median interquartile range [IQR], 40 minutes [20–60] vs 60 minutes [40–85]; $P = 0.008$), without clinically significant overshoot hypotension, in a small RCT of 60 pregnant women.[22] Guidance for the obstetric anesthesiologist on how to safely minimize maternal hemodynamic changes during induction of general anesthesia in preeclamptic patients was provided by Yoo et al.[23] These investigators determined that remifentanil (ED_{95} = 1.34 μg/kg) attenuated the blood pressure and heart rate response to tracheal intubation in patients with severe preeclampsia who were induced using 5 mg/kg of thiopental and 1.5 mg/kg of succinylcholine. Side effects included transient, self-limited fetal respiratory depression.

The timing of preeclampsia onset was found to be correlated with the degree of maternal and fetal morbidity. Early-onset preeclampsia (<34 0/7 weeks' gestational age) was associated with a substantially increased risk of perinatal death or severe neonatal morbidity (aOR, 16.4; 95% CI, 14.5–18.6) and was more strongly associated with risk factors such as chronic hypertension and African race compared with later-onset disease (aOR, 2.0; 95% CI, 1.8–2.3).[24] The maternal morbidity associated with hypertensive disorders of pregnancy is more generalized than previously thought. All pregnancy-related hypertension, including gestational hypertension, was associated with increased risk for future maternal cardiovascular and renal disease, ischemic stroke, and fatal myocardial infarctions in a population-based cohort study of >10,000 women with an average of 39 years of follow-up.[25] This study controlled for prepregnancy risk factors (e.g., obesity and smoking), but not for the effect of antihypertensive therapy or postpartum risk factors.

Maternal Sepsis

Bauer et al.[26] studied maternal sepsis (occurring in 1 per 3333 deliveries) and found that the odds of acquiring the severe form with acute organ dysfunction, hypotension, or hypoperfusion (occurring in l per 10,823 deliveries) and sepsis-related death (occurring in 1 per 105,263 deliveries) increased by 10% per year in the United States from 1998 to 2008. This analysis of Nationwide Inpatient Sample data revealed that common infections and microorganisms are responsible for maternal sepsis; pneumonia and genitourinary infections each comprised 30%, and uterine infections, another 25%. The most common pathogens were *Escherichia coli* (27%), *Staphylococcal* (22%), and *Streptococcal* (20%) bacteria. Although risk factors for severe sepsis were identified, including advanced maternal age, African race, Medicaid insurance, retained products of conception, premature rupture of membranes, multiple gestations, congestive heart failure, systemic lupus erythematosus, and chronic renal or liver disease, none had a population attributable risk fraction of >6%. Thus, the onus is on the obstetric care providers to be vigilant and proactive in diagnosing impending sepsis in patients who may otherwise appear to have a more benign disease course.

Anesthesia-Related Morbidity and Mortality

Anesthesia-related maternal mortality has continued to decrease, in part due to the pervasive and successful use of neuraxial anesthesia.[27] Failed tracheal intubation in an obstetric general anesthetic is typically defined as the inability to achieve intubation during a rapid sequence induction, requiring a failed intubation drill. Recent data confirm an event rate of 1 failed intubation per 244 successful intubations in obstetrics, which is approximately 10 times that in the general surgical population.[28] Fortunately, in this series of failed and successful general anesthetics in United Kingdom between 2008 and 2010, there were no maternal deaths. The classic laryngeal mask airway was successfully used as a rescue device in the majority (68%) of the intubation failure cases. One of the failed intubation patients required a surgical airway, and 4 had pulmonary aspiration of gastric contents, all with good clinical outcomes. The risk of intubation failure was increased when a junior anesthetist was caring for the patient without a senior consultant present (OR, 2.42; 95% CI, 1.06–5.52, $P = 0.036$) and in patients with advanced maternal age (OR, 1.07; 95% CI, 1.01–1.14, $P = 0.01$). In addition, there was a 7% increase in the risk of failed intubation for each 1 kg/m^2 increase in the patient's body mass index (BMI) (kg/m^2).

Postpartum respiratory compromise, particularly in obese patients, is an important cause of anesthesia-related maternal mortality[29] that was investigated in a retrospective review of 5036 cesarean deliveries.[30] The mean BMI was 34 kg/m^2, and the BMI was >40 kg/m^2 in 17% of the study cohort. It is reassuring that the standard, post–cesarean delivery multimodal pain regimen of spinal or epidural morphine with oral oxycodone or nonsteroidal anti-inflammatory medications (NSAIDS) for breakthrough pain was not associated with respiratory depression requiring naloxone therapy or rapid response team intervention. However, minor oxygen desaturations and other measures of respiratory compromise were not recorded.

When maternal cardiac arrest occurs and resuscitation does not return spontaneous circulation by 5 minutes, perimortem cesarean delivery is indicated to improve maternal and fetal outcome.[31] If the arrest occurs in the labor room, then it is plausible that transferring the patient to the operating room might be beneficial (e.g., to maximize sterility and optimize lighting and access to supplies). To analyze this rare and critical event, Lipman et al.[32] measured the effect of simulated patient transfer from the labor to operating room on the efficacy of chest compressions. The percentage of correctly delivered compressions (i.e., those with sufficient depth, correct sternal hand placement, and without release/leaning) was significantly degraded when the patient was moved from the labor room to the operating room, even after arrival in the operating room (median [IQR] correct compressions, 32% [10–63] for the transport group versus 93% [58–100] for the stationary group; $P = 0.002$). Interruptions in resuscitation efforts were observed in virtually all (92%) of the transport group and only 7% of the stationary group ($P < 0.001$) drills. Tidal volume was also compromised in the transport group compared with the stationary group (median [IQR], 270 mL [166–430] vs 390 mL [232–513]; $P = 0.03$). As chest compressions are critical to successful resuscitation,[31] these results provide compelling support for performing cesarean delivery at the site of the arrest.

Fetal Outcomes

Several studies in 2013 provided insight into potential threats to fetal well-being and the role obstetric and anesthetic care providers play to ameliorate them.

Preterm Labor and Delivery

Recognizing that preterm birth is a leading cause of death in children under 5 years old,[33] several collaborative international initiatives set ambitious goals for decreasing the preterm birth rate.[34] In their analysis of 39 United Nations countries with high achievement in health, education, and economic standards, Chang et al.[35] concluded that nonmedically indicated cesarean delivery and induction of labor accounted for approximately 50% of the increase in these countries (20% in the United States). Compared to their European counterparts, the United States had a higher preterm birth rate and a smaller fraction of identifiable and modifiable causes. The authors estimated a 5% average decrease in the preterm birth rate per country was realistic, falling short of the overall 50% reduction by 2025 targeted by the March of Dimes in their "Born Too Soon" goal. Although resulting in only 58,000 fewer preterm births per year, this 5% estimated reduction would generate an annual savings of $3 billion U.S. dollars. In a study of 1.6 million births in Sweden, obese parturients were identified as being at particular risk for extremely preterm birth (22–27 weeks' gestational age).[36] Compared to women with normal BMI (18.5 to <25 kg/m^2), overweight (BMI ≥ 25 kg/m^2), and grade 4 obese (BMI ≥ 40 kg/m^2), pregnant women had an increased odds of delivering extremely preterm neonates (aOR, 1.26; 95% CI, 1.15–1.37 and aOR, 2.99; 95% CI, 2.28–3.92, respectively).

Some controversies surrounding the optimal management of pregnant women with preterm labor or preterm birth were resolved in 2013. Although a short course of tocolytic therapy with beta-agonists or oxytocin antagonists transiently prolongs pregnancy,[37,38] the Assessment of Perinatal Outcome after Sustained Tocolysis in Early Labour (APOSTEL)-II RCT of 400 women demonstrated no additional benefit of maintenance tocolysis with oral nifedipine compared to placebo in reducing a composite measure of chronic lung disease, neonatal sepsis, severe intraventricular hemorrhage, periventricular leukomalacia >grade 1, necrotizing enterocolitis, or perinatal death relative risk [RR], 0.87; 95% CI, 0.53–1.45; and risk difference, 1.8%; 95% CI, −4.7% to 8.3%).[39] In contrast, a repeat course of maternal steroid administration after 7 days in women with preterm labor who remain pregnant was shown to significantly decrease respiratory distress syndrome (aRR, 0.83; 95% CI, 0.75–0.91) and a composite of serious fetal morbidity (death, severe respiratory distress syndrome, and intraventricular hemorrhage) (aRR, 0.84; 95% CI, 0.75–0.94) in fetuses <34 weeks.[40] There is also incremental value in receiving a partial course of therapy if a full course is not feasible. A repeat course is not, however, recommended for women with premature, preterm rupture of membranes,[41] and the preferred choice of corticosteroid remains unknown.[42]

Conclusive data have been lacking to guide oxygen therapy for extremely preterm newborns given the benefits (e.g., less periodic apnea and severe neonatal morbidity) and risks (e.g., retinopathy of prematurity and bronchopulmonary dysplasia) of exposure to high concentrations of inspired oxygen.[43] The international Benefits of Oxygen Saturation Targeting (BOOST) II collaborative of 3 trials in 54 hospitals randomized 2448 preterm babies (22–28 weeks' gestational age) to either low-target oxygen saturation of 85% to 89% or high-target oxygen saturation of 91% to 95%.[44] The study was terminated prematurely after an interim analysis revealed an alarming increase in fetal death in the low-target oxygen saturation group (23.1% vs 15.9%; aRR, 1.45; 95% CI, 1.15–1.84; $P = 0.002$). In their accompanying editorial, Polin and Bateman[45] commended this rigorous investigation but highlighted that the significant between-group difference in mortality was found after a revision of the oxygen saturation calibration algorithm at 2 sites. While awaiting the results of a planned meta-analysis of these and other relevant trials, they espoused targeting an oxygen saturation target between 90% and 95% in these very preterm infants.

The American College of Obstetricians and Gynecologists has concluded that a nonmedically indicated delivery at < 39 0/7 weeks' gestational age are not appropriate.[46] Deliveries at 37 0/7 to 38 6/7 weeks' gestational age that were previously indicated, because of suspected macrosomia, documented fetal lung maturity, or well-controlled gestational diabetes, are no longer justifiable. By way of explanation, they have cited a higher risk of adverse neonatal outcome (composite of adverse respiratory outcomes, newborn sepsis, seizures, or necrotizing enterocolitis) for neonates delivered at 37 0/7 to 6/7 weeks' or 38 0/7 to 6/7 weeks' gestational age (aOR, 1.5; 95% CI, 1.3–1.7 and aOR, 2.1; 95% CI, 1.7–2.5, respectively; P value for trend <0.001) compared to those that delivered at 39 weeks' gestational age.[47]

Mode of Delivery

Vaginal delivery (between 39 0/7 weeks' and 40 6/7 weeks' gestational age) is considered to be superior to cesarean delivery without maternal or fetal indications because it causes less subsequent uterine rupture or placenta previa or accreta, less neonatal respiratory morbidity, and shorter maternal length of stay.[48] ACOG recommends that if a patient still desires a cesarean delivery on "maternal request," then it *not* be performed (a) before 39 weeks, (b) because of inadequate pain control during labor, or (c) if multiple children are desired.

Barrett et al.[49] challenged the perceived benefits of delivering twins (first twin in the cephalic position) between 32 0/7 and 38 6/7 weeks' gestational age by cesarean delivery by randomizing women to either cesarean delivery or vaginal delivery with a cesarean *only if it was deemed to be obstetrically necessary at the time of delivery.* Participating obstetricians were proficient in vaginal breech deliveries. Neither maternal nor fetal death, nor serious maternal or fetal morbidity, was statistically different based on delivery mode. However, 44% of patients randomized to the vaginal delivery group ultimately had cesarean deliveries, suggesting that cesarean deliveries for these twins are likely to persist.

In Utero Exposures

Ondansetron is a widely prescribed antiemetic drug used during pregnancy. Using propensity score matching of a cohort of over 600,000 women who received ondansetron versus other antiemetic medications for severe nausea and vomiting, the safety of ondansetron use during pregnancy

was confirmed.[50] There were no significantly increased perinatal risks for any major birth defect in the first trimester (adjusted prevalence OR, 1.12; 95% CI, 0.69–1.82), or for preterm delivery before 37 weeks' gestational age (adjusted prevalence OR, 0.90; 95% CI, 0.66–1.25). Similarly, there was no increased risk for spontaneous abortion associated with exposure during the first and second trimesters, or associated with exposures throughout pregnancy.

The consequences of in utero exposure to opioids were critically examined in data from the Slone Epidemiology Center Birth Defects Study.[51] At 6 months postpartum, mothers of 305 babies with neural tube defects, mothers of 13,405 babies with other malformations, and over 7000 normal controls were queried retrospectively about sociodemographic factors and exposures during pregnancy, including opioid use (type and timing) within the 2 months after their last menstrual period. There were 15 different opioids reported for 7 categories of indications. The analysis showed a 2.2-fold increase in neural tube defects (95% CI, 1.2–4.2) in opioid-exposed babies after adjustment for confounders such as race–ethnicity, maternal age, maternal comorbidities, and other ingestions for a neural tube defect prevalence of 5.9 per 10,000 births. When codeine versus noncodeine opioid exposures were compared, the overall ORs were essentially unchanged, although the risk for spina bifida was increased in the noncodeine group (aOR, 2.8; 95% CI, 1.3–6.3). These odds of neural tube defects due to opioids were attenuated (aOR, 1.9; 95% CI, 1.0–3.4) when the index cohort was compared the mothers with babies who had other malformations (to minimize the impact of recall bias). Proposed causal mechanisms include the role of endogenous opioids in organogenesis and the interference of exogenous opioids in these processes. The lack of detail about opioid dosing and the potential for confounding by comorbidities and recall bias are limitations of this study which call for additional research. However, given the recent increase in opioid use and dependence during pregnancy,[52] and previous reports associating in utero opioid exposure in the first trimester with spina bifida and other congenital birth defects,[53] alternative forms of analgesia or anesthesia for pregnant women should be considered.

Fetal Monitoring

Despite widespread use of continuous, compared to intermittent, fetal heart rate monitoring, a Cochrane meta-analysis of 13 RCTs or quasi-RCTs confirmed that neither the risk of fetal cerebral palsy (aRR, 1.75; 95% CI, 0.84–3.63) nor fetal death (aRR, 0.86; 95% CI: 0.59–1.23) was significantly decreased with continuous monitoring.[54] The neonatal seizure risk was decreased (aRR, 0.50; 95% CI, 0.31–0.80), although the clinical significance of this finding is unclear. Either cesarean delivery or assisted vaginal delivery was more likely when continuous monitoring was used (aRR, 1.63; 95% CI, 1.29–2.07 and aRR, 1.15; 95% CI, 1.01–1.33, respectively). In a population-based, retrospective study between 1990 and 2004, the authors associated the decrease in neonatal morbidity and mortality rates with the temporal increase in the use of continuous fetal heart rate monitoring.[55] This association was likely confounded by concurrent changes in obstetrical practice, including antenatal corticosteroid and surfactant use, the adoption of ultrasound for accurate gestational age estimation, and other unmeasured confounders.[56,57]

Anesthetic Outcomes

Labor Analgesia

Guidance for maximizing the success of neuraxial labor analgesia was enhanced by Thangamuthu et al.; they constructed a standardized definition of epidural analgesia failure using the Delphi method. This definition may be useful in clinical practice, research, and quality improvement.[58] In their subsequent single-center review of 1521 epidural anesthetics, these investigators found an astonishing 23% of epidural analgesia failed according to 1 or more of their criteria:

1. Inadequate analgesia at 45 minutes from the start of the epidural procedure;
2. Catheter re-site required or technique abandoned;
3. Unintentional dural puncture;
4. Patient dissatisfied with epidural labor analgesia at follow-up visit with obstetric provider.

The lowest failure rates were associated with catheter placement by more senior trainees (≥5 years of experience), and with epidural catheter insertions 5–5.9 cm into the epidural space compared to <5 cm or >6 cm. Time of day, duration of labor, cervical dilation, or patient position at time of placement did not affect failure rate. The most common reason for failure was inadequate analgesia at 45 minutes, suggesting that routine patient checks after epidural analgesia initiation and timely and reliable catheter placement should be a regular part of obstetric anesthesia practice.

Ultrasonography, typically with a low-frequency curved array probe, was confirmed to be a useful tool for epidural catheter placement and dural punctures in a 2013 meta-analysis.[59] Fourteen RCTs with mixed obstetric–surgical populations and with very low heterogeneity were analyzed; the use of ultrasound reduced the risk of procedure failure compared to the landmark palpation method (RR, 0.21; 95% CI, 0.10–0.43; $P < 0.001$). Traumatic procedures (RR, 0.27; 95% CI, 0.11–0.67; $P = 0.005$), insertion attempts (mean difference, −0.44; 95% CI, −0.64 to −0.24; $P < 0.001$), and number of needle redirections (mean difference, −1.00; 95% CI, −1.24 to −0.75; $P < 0.001$) also decreased. In a separate study of 60 obese parturients in whom epidural catheter failure rate can be as high as 42%,[60] Sahota et al.[61] showed that the distance from the skin to the epidural space can be accurately estimated in either the paramedian sagittal oblique or the transverse median ultrasound view, provided the tissue is not compressed during the measurement. As most investigations of ultrasound use for neuraxial procedures have been performed by a limited number of experienced clinicians, it remains to be seen whether widespread adoption of this technology for all neuraxial anesthetic techniques will occur and improve outcomes.

In a single-center RCT with 800 women in a private practice setting, Gambling et al.[62] investigated whether combined spinal–epidural analgesia (CSE) provided superior labor analgesia to epidural analgesia. Patients in the epidural group received 10 mL 0.125% bupivacaine with 2 μg/mL fentanyl through the epidural needle, and 5 mL of the mixture through the epidural catheter. The CSE group received 2.5 mL of the bupivacaine and fentanyl mixture through a spinal needle before epidural catheter placement. Both groups were maintained with patient-controlled

epidural analgesia (PCEA). Compared to the epidural group, the CSE patients had statistically, but not necessarily clinically, significantly lower pain scores in the first hour (1.4 vs 1.9 using a 0–10 verbal pain scale; $P < 0.001$). The second stage and delivery labor pain scores were equivalent. Although there were fewer anesthesiologist top-up doses needed in the CSE group, there were more side effects, specifically maternal pruritus and fetal bradycardia. The epidural catheter failure rate was very low (1%–2%) and did not differ significantly between groups. As highlighted in the accompanying editorial, this study confirmed that both CSE and epidural analgesia are excellent options for labor pain management.[63] Further studies are needed to investigate whether epidural catheters placed as part of CSE techniques are more likely to function as successful operative anesthetics for cesarean deliveries compared with catheters placed a part of a traditional epidural technique.

Labor epidural analgesia delivered by a timed intermittent bolus (epidural pump programmed to deliver a bolus at regular intervals) was shown to improve maternal satisfaction (on a 100-mm visual analog scale; mean difference, 7.0 mm; 95% CI, 6.2–7.8; $P < 0.0001$) and moderately decrease local anesthetic consumption when compared to continuous infusion with or without PCEA (mean difference, −1.2 mg bupivacaine equivalent per hour; 95% CI, −2.2 to −0.3; $P < 0.0001$) in a systematic review of 9 RCTs with low risk of bias.[64] Sia et al.[65] varied the frequency of automated boluses in response to the patient's needs. One hundred and two patients with CSE analgesia were randomized to either a conventional or novel PCEA group with automated mandatory boluses administered 1 to 4 times per hour, depending on individual patients' recent analgesic demand doses. The automated mandatory bolus group had (a) greater satisfaction, (b) a 4-fold decrease in the incidence of breakthrough pain requiring anesthesiologist top-up doses (5.9% vs 23.5%, $P = 0.023$), and (c) equivalent total anesthetic consumption compared to the PCEA conventional group. The authors speculated that the higher satisfaction might have been because those patients received more machine delivered boluses in advanced labor. It is reassuring that the improved analgesia was not associated with a difference in the duration of the second stage of labor, mode of delivery, or neonatal outcomes, although the study was underpowered to formally investigate these outcomes.

Postdural puncture headache (PDPH) remains one of the most common complications of obstetric neuraxial anesthesia.[66] A recent Cochrane review of 10 RCTs found the study populations (both obstetric and non-obstetric) and study designs too heterogeneous for a meta-analysis to assess whether prophylactic medical therapy successfully reduced the number of participants affected by PDPH after either intentional or unintentional dural puncture.[67] Results from a single trial suggest that 1 dose of 1 mg IV cosyntropin administered after delivery was the most promising therapy for reducing the number of patients with PDPH of any severity (aRR, 0.49; 95% CI, 0.31–0.79) and had a more favorable side effect profile than epidural or spinal morphine, oral caffeine, spinal fentanyl, oral caffeine, rectal indomethacin, IV aminophylline, or IV dexamethasone. However, a larger RCT that controls for baseline severity of PDPH symptoms is needed to confirm this effect.

Cesarean Delivery Anesthesia and Postoperative Pain Management

An investigation of spinal anesthesia for cesarean delivery of fetuses with compromised umbilical circulation lends support to the safety of neuraxial anesthesia in women with vulnerable fetuses.[68] Forty patients with growth restricted fetuses and impaired Doppler flow on umbilical artery ultrasound were randomized to receive low-dose spinal anesthesia (hyperbaric bupivacaine 8 mg with fentanyl 20 μg) or general anesthesia for cesarean delivery. The umbilical artery base deficit, a primary measure of the fetal metabolic condition at birth, was not significantly different between the anesthetic groups, although the umbilical artery pH was lower in the spinal versus the general anesthesia group (mean ± SD, 7.23 ± 0.06 vs 7.27 ± 0.04; $P = 0.01$). There were also no significant differences in Apgar scores at 1 and 5 minutes or in the need for fetal resuscitation between groups. Given the small sample size and the low spinal bupivacaine dose, further investigation is needed to generalize these results.

Persistent, inadequately treated postpartum pain is associated with an increased risk of maternal depression and adverse neonatal outcomes[69]; thus, investigators collaborated to identify patients at high risk for postpartum pain and to expand the analgesic armamentarium. Pan et al.[70] created a preoperative tool to predict the top 20th percentile of patients with post–cesarean delivery pain scores based on patient (a) anxiety level, (b) anticipated pain, and (c) anticipated postoperative analgesic needs assessed in the preoperative period. The model had moderate correlation ($r = 0.24$–0.33; $P < 0.001$) with risk for postpartum pain; patients in the top 20th percentile of postoperative pain with movement tended to be younger, less educated, and more often single than the remainder of the cohort. In a separate investigation, the language used to describe postoperative sensations was found to influence the report of pain and the request for pain medication, particularly when negative verbal suggestions were used.[71] Chooi et al. explored this nocebo effect in their RCT of 300 women receiving neuraxial or general anesthesia for cesarean delivery. Patients who were asked postoperatively about "comfort" and "healing" reported less "bother" and other negative aspects of the surgery than patients asked about "pain." They were also less likely to request additional pain medication. The limitations of this study included the lack of long-term follow-up and the assumption that "comfort" and "pain" scores were mathematically reciprocal (i.e., that on a scale from 1 to 10, a pain score of "3" out of 10 corresponded to comfort score of "7" out of 10).

Improving spinal analgesia for cesarean delivery was the objective of the double-blind RCT of 80 patients conducted by Subedi et al.[72] These investigators reported that adding 10 mg intrathecal tramadol versus 10 μg intrathecal fentanyl to hyperbaric bupivacaine (10 mg) increased the median (IQR) duration of postoperative analgesia (300 minutes (240–360) vs 260 minutes (233–300), respectively; $P = 0.02$). The intrathecal tramadol group also had less shivering (5% vs 43% incidence; $P = 0.03$), and there was no negative impact on neonatal Apgar scores, fetal acid-base status, or other neonatal scoring. However, adequate

safety studies for intrathecal tramadol have not yet been published. In another study, half (i.e., 1.5 mg) of the usual 3.0 mg epidural morphine dose was found to provide satisfactory postoperative pain relief after cesarean delivery while reducing the side effects.[73] The median difference between the 24-hour opioid (IV morphine-equivalent) consumption between the 2 groups was 0 mg (1-sided 95% CI, 2.5 mg), clearly within the predetermined 3.33 mg morphine-equivalent, noninferiority margin. There were no significant differences between groups in pain scores or in satisfaction, and there was less frequent pruritus and nausea in the 1.5-mg group. Although these results support the use of the lower neuraxial opioid dose, subtle differences in analgesic needs may have been underappreciated, as patients were unable to self-administer additional opioid and relied on their nurse to do so. Beatty et al.[74] provided guidance for the use of intrathecal (preservative-free) hydromorphone for postoperative analgesia as an alternative to preservative-free morphine, which has been intermittently unavailable in the past several years. In their retrospective review, 38 patients who received 0.04 mg hydromorphone after elective cesarean delivery were compared with 76 patients who received 0.1 mg morphine. There were no significant differences in the frequency of opioid-related complications (primary outcome), pain scores, or additional opioid consumption.

Adding bilateral transversus abdominis plane (TAP) blocks to the multimodal post–cesarean delivery pain medication regimen of intrathecal morphine, NSAIDS or acetaminophen plus opioids for breakthrough pain did not confer long-lasting analgesic benefits in 2 RCTs.[75,76] Pain scores with movement at 24 hours were not significantly different in a study that compared the effects of high-dose (3.0 mg/kg of ropivacaine) and low-dose (1.5 mg/kg of ropivacaine) TAP blocks performed immediately postoperatively and a saline control group.[75] The lower pain scores with movement at 6 and 12 hours in the high-dose local anesthetic TAP group suggest transient analgesic effects that did not outlast the local anesthetic duration of action. Bilateral TAP blocks with an intermediate local anesthetic concentration (20 mL of 0.5% ropivacaine in 51 patients versus saline) yielded similar results.[76] These studies suggest that TAP blocks may be most beneficial in patients with relative contraindications to neuraxial anesthesia/analgesia. When serum drug concentrations were measured in parturients receiving TAP blocks (2.5 mg/kg diluted in 40 mL saline) for post–cesarean delivery pain management, the total plasma concentrations of ropivacaine exceeded the potentially toxic threshold (2.2 μg/mL) in 40% of the patients within the first hour.[77] Several of these patients were obese, and 3 had transient symptoms of local anesthetic systemic toxicity (perioral/tongue paraesthesia, metallic taste, or slurred speech). This finding suggests that choosing local anesthetics with a favorable toxicity profile (e.g., ropivacaine) and a needle insertion site that maximizes local anesthetic spread is particularly important in these patients.

Effective neuraxial anesthesia can be used to increased comfort and success of external cephalic version (ECV) for nonvertex fetal presentation.[78] Carvalho et al.[79] presented a novel view of the way that obstetric anesthesiologists add value to ECV by calculating the potential cost savings when neuraxial anesthesia is used. This analysis factored in the likelihood of successful version and the relative cost of subsequent vaginal versus cesarean delivery. Their conclusion was that ECV with neuraxial anesthesia not only increases the chances of a vaginal delivery but is also cost-effective (average cost savings = $276 per delivery; 2.5th to 97.5th prediction interval: −$720 to $112).[79]

CONCLUSIONS

This review highlights the broad range of influential work published during 2013 aimed at better understanding potentially modifiable threats to maternal and fetal safety and the influence of the anesthesiologists' peridelivery care. Obstetric anesthesiologists have been the investigators in many of the significant advances in preeclampsia, maternal morbidity and mortality, the basic science of pregnancy, anesthetic practice, and education during calendar year 2013. This author would like to express her appreciation to all the colleagues who contributed to maternal and fetal health in 2013, regardless of whether their studies were included in this review, as we have benefited tremendously from their contributions.

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REFERENCES

1. Saucedo M, Deneux-Tharaux C, Bouvier-Colle M-H. Ten years of confidential inquiries into maternal deaths in France, 1998–2007. Obstet Gynecol 2013;122:752–60
2. Lewis G. Centre for maternal and child health enquiries. Saving mothers' lives: reviewing maternal deaths to make motherhood safer: 2006–2008. The eighth report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. Br J Obstet Gynaecol 2011;118:1–203
3. Sullivan E, Hall B, King J. Maternal Deaths in Australia 2003–2005. Maternal Deaths Series No. 3. Cat. no. PER 42. Sydney, Australia: AIHW National Perinatal Statistics Unit, 2007
4. Berg CJ, Callaghan WM, Syverson C, Henderson Z. Pregnancy-related mortality in the United States, 1998 to 2005. Obstet Gynecol 2010;116:1302–9
5. Lisonkova S, Liu S, Bartholomew S, Liston RM, Joseph KS; Maternal Health Study Group of the Canadian Perinatal Surveillance System. Temporal trends in maternal mortality in Canada II: estimates based on hospitalization data. J Obstet Gynaecol Can 2011;33:1020–30
6. Philibert M, Deneux-Tharaux C, Bouvier-Colle MH. Can excess maternal mortality among women of foreign nationality be explained by suboptimal obstetric care? BJOG 2008;115:1411–8
7. Aylin P, Bottle A, Majeed A. Use of administrative data or clinical databases as predictors of risk of death in hospital: comparison of models. BMJ 2007;334:1044

8. Southern DA, Quan H, Ghali WA. Comparison of the Elixhauser and Charlson/Deyo methods of comorbidity measurement in administrative data. Med Care 2004;42:355–60
9. Bateman BT, Mhyre JM, Hernandez-Diaz S, Huybrechts KF, Fischer MA, Creanga AA, Callaghan WM, Gagne JJ. Development of a comorbidity index for use in obstetric patients. Obstet Gynecol 2013;122:957–65
10. Kramer MS, Berg C, Abenhaim H, Dahhou M, Rouleau J, Mehrabadi A, Joseph KS. Incidence, risk factors, and temporal trends in severe postpartum hemorrhage. Am J Obstet Gynecol 2013;209:449.e1–7
11. Tunçalp O, Souza JP, Gülmezoglu M; World Health Organization. New WHO recommendations on prevention and treatment of postpartum hemorrhage. Int J Gynaecol Obstet 2013;123:254–6
12. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, Fries D, Görlinger K, Haas T, Imberger G, Jacob M, Lancé M, Llau J, Mallett S, Meier J, Rahe-Meyer N, Samama CM, Smith A, Solomon C, Van der Linden P, Wikkelsø AJ, Wouters P, Wyffels P. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol 2013;30:270–382
13. Abdel-Aleem H, Alhusaini TK, Abdel-Aleem MA, Menoufy M, Gülmezoglu AM. Effectiveness of tranexamic acid on blood loss in patients undergoing elective cesarean section: randomized clinical trial. J Matern Fetal Neonatal Med 2013;26:1705–9
14. Cook L, Roberts I; WOMAN Trial Collaborators. Postpartum haemorrhage and the WOMAN trial. Int J Epidemiol 2010;39:949–50
15. Elagamy A, Abdelaziz A, Ellaithy M. The use of cell salvage in women undergoing cesarean hysterectomy for abnormal placentation. Int J Obstet Anesth 2013;22:289–93
16. Rogers WK, Wernimont SA, Kumar GC, Bennett E, Chestnut DH. Acute hypotension associated with intraoperative cell salvage using a leukocyte depletion filter during management of obstetric hemorrhage due to amniotic fluid embolism. Anesth Analg 2013;117:449–52
17. Arriaga AF, Bader AM, Wong JM, Lipsitz SR, Berry WR, Ziewacz JE, Hepner DL, Boorman DJ, Pozner CN, Smink DS, Gawande AA. Simulation-based trial of surgical-crisis checklists. N Engl J Med 2013;368:246–53
18. Wallis AB, Saftlas AF, Hsia J, Atrash HK. Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States, 1987-2004. Am J Hypertens 2008;21:521–6
19. American College of Obstetricians and Gynecologists Task Force on Hypertension. Hypertension in pregnancy. Obstet Gynecol. 2013;122:1122–31
20. Foo L, Bewley S, Rudd A. Maternal death from stroke: a thirty year national retrospective review. Eur J Obstet Gynecol Reprod Biol 2013;171:266–70
21. Duley L, Meher S, Jones L. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database Syst Rev 2013;7:CD001449
22. Shekhar S, Sharma C, Thakur S, Verma S. Oral nifedipine or intravenous labetalol for hypertensive emergency in pregnancy: a randomized controlled trial. Obstet Gynecol 2013;122:1057–63
23. Yoo KY, Kang DH, Jeong H, Jeong CW, Choi YY, Lee J. A dose-response study of remifentanil for attenuation of the hypertensive response to laryngoscopy and tracheal intubation in severely preeclamptic women undergoing caesarean delivery under general anaesthesia. Int J Obstet Anesth 2013;22:10–8
24. Lisonkova S, Joseph KS. Incidence of preeclampsia: risk factors and outcomes associated with early- versus late-onset disease. Am J Obstet Gynecol 2013;209:544.e1–544.e12
25. Männistö T, Mendola P, Vääräsmäki M, Järvelin MR, Hartikainen AL, Pouta A, Suvanto E. Elevated blood pressure in pregnancy and subsequent chronic disease risk. Circulation 2013;127:681–90
26. Bauer ME, Bateman BT, Bauer ST, Shanks AM, Mhyre JM. Maternal sepsis mortality and morbidity during hospitalization for delivery: temporal trends and independent associations for severe sepsis. Anesth Analg 2013;117:944–50
27. Hawkins JL, Chang J, Palmer SK, Gibbs CP, Callaghan WM. Anesthesia-related maternal mortality in the United States: 1979-2002. Obstet Gynecol 2011;117:69–74
28. Quinn AC, Milne D, Columb M, Gorton H, Knight M. Failed tracheal intubation in obstetric anaesthesia: 2 yr national case-control study in the UK. Br J Anaesth 2013;110:74–80
29. Carvalho B. Respiratory depression after neuraxial opioids in the obstetric setting. Anesth Analg 2008;107:956–61
30. Crowgey TR, Dominguez JE, Peterson-Layne C, Allen TK, Muir HA, Habib AS. A retrospective assessment of the incidence of respiratory depression after neuraxial morphine administration for postcesarean delivery analgesia. Anesth Analg 2013;117:1368–70
31. Vanden Hoek TL, Morrison LJ, Shuster M, Donnino M, Sinz E, Lavonas EJ, Jeejeebhoy FM, Gabrielli A. Part 12: cardiac arrest in special situations: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122:S829–61
32. Lipman SS, Wong JY, Arafeh J, Cohen SE, Carvalho B. Transport decreases the quality of cardiopulmonary resuscitation during simulated maternal cardiac arrest. Anesth Analg 2013;116:162–7
33. Liu L, Johnson HL, Cousens S, Perin J, Scott S, Lawn JE, Rudan I, Campbell H, Cibulskis R, Li M, Mathers C, Black RE; Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality: an updated systematic analysis for 2010 with time trends since 2000. Lancet 2012;379:2151–61
34. March of Dimes, PMNCH, Save the Children, WHO. Born Too Soon: The Global Action Report on Preterm Birth. Howson C, Kinney M, Lawn J, eds. Geneva: World Health Organization, 2012
35. Chang HH, Larson J, Blencowe H, Spong CY, Howson CP, Cairns-Smith S, Lackritz EM, Lee SK, Mason E, Serazin AC, Walani S, Simpson JL, Lawn JE; Born Too Soon preterm prevention analysis group. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. Lancet 2013;381:223–34
36. Cnattingius S, Villamor E, Johansson S, Edstedt Bonamy AK, Persson M, Wikström AK, Granath F. Maternal obesity and risk of preterm delivery. JAMA 2013;309:2362–70
37. Antenatal corticosteroids revisited: repeat courses. NIH Consens Statement 2000;17:1–18
38. Conde-Agudelo A, Romero R, Kusanovic JP. Nifedipine in the management of preterm labor: a systematic review and meta-analysis. Am J Obstet Gynecol 2011;204:134.e1–e20
39. Roos C, Spaanderman ME, Schuit E, Bloemenkamp KW, Bolte AC, Cornette J, Duvekot JJ, van Eyck J, Franssen MT, de Groot CJ, Kok JH, Kwee A, Merién A, Nij Bijvank B, Opmeer BC, Oudijk MA, van Pampus MG, Papatsonis DN, Porath MM, Scheepers HC, Scherjon SA, Sollie KM, Vijgen SM, Willekes C, Mol BW, van der Post JA, Lotgering FK; APOSTEL-II Study Group. Effect of maintenance tocolysis with nifedipine in threatened preterm labor on perinatal outcomes: a randomized controlled trial. JAMA 2013;309:41–7
40. Crowther CA, McKinlay CJ, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database Syst Rev 2013:CD003935
41. American College of Obstetricians and Gynecologists. ACOG Practice bulletins no. 139: premature rupture of membranes. Obstet Gynecol 2013;122:918–30
42. Brownfoot FC, Gagliardi DI, Bain E, Middleton P, Crowther CA. Different corticosteroids and regimens for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2013;8:CD006764
43. Solis A, Harrison G, Shaw BN. Assessing oxygen requirement after discharge in chronic lung disease: a survey of current practice. Eur J Pediatr 2002;161:428–30
44. Stenson BJ, Tarnow-Mordi WO, Darlow BA, Simes J, Juszczak E, Askie L, Battin M, Bowler U, Broadbent R, Cairns P, Davis PG, Deshpande S, Donoghoe M, Doyle L, Fleck BW, Ghadge A, Hague W, Halliday HL, Hewson M, King A, Kirby A, Marlow N, Meyer M, Morley C, Simmer K, Tin W, Wardle SP,

Brocklehurst P. Oxygen saturation and outcomes in preterm infants. N Engl J Med 2013;368:2094–104
45. Polin RA, Bateman D. Oxygen-saturation targets in preterm infants. N Engl J Med 2013;368:2141–2
46. American College of Obstetricians and Gynecologists. ACOG Committee opinion no. 561: nonmedically indicated early-term deliveries. Obstet Gynecol 2013;121:911–5
47. Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW, Moawad AH, Caritis SN, Meis PJ, Wapner RJ, Sorokin Y, Miodovnik M, Carpenter M, Peaceman AM, O'Sullivan MJ, Sibai BM, Langer O, Thorp JM, Ramin SM, Mercer BM; Eunice Kennedy Shriver NICHD Maternal-Fetal Medicine Units Network. Timing of elective repeat cesarean delivery at term and neonatal outcomes. N Engl J Med 2009;360:111–20
48. American College of Obstetricians and Gynecologists. ACOG Committee opinion no. 559: cesarean delivery on maternal request. Obstet Gynecol 2013;121:904–7
49. Barrett JF, Hannah ME, Hutton EK, Willan AR, Allen AC, Armson BA, Gafni A, Joseph KS, Mason D, Ohlsson A, Ross S, Sanchez JJ, Asztalos EV; Twin Birth Study Collaborative Group. A randomized trial of planned cesarean or vaginal delivery for twin pregnancy. N Engl J Med 2013;369:1295–305
50. Pasternak B, Svanström H, Hviid A. Ondansetron in pregnancy and risk of adverse fetal outcomes. N Engl J Med 2013;368:814–23
51. Yazdy MM, Mitchell AA, Tinker SC, Parker SE, Werler MM. Periconceptional use of opioids and the risk of neural tube defects. Obstet Gynecol 2013;122:838–44
52. Salihu HM, Mogos MF, Salinas-Miranda AA, Salemi JL, Whiteman VE. National trends in maternal use of opioid drugs among pregnancy-related hospitalizations in the United States, 1998 to 2009. Am J Perinatol 2014: doi: 10.1055/s-0034-1384642
53. Broussard CS, Rasmussen SA, Reefhuis J, Friedman JM, Jann MW, Riehle-Colarusso T, Honein MA; National Birth Defects Prevention Study. Maternal treatment with opioid analgesics and risk for birth defects. Am J Obstet Gynecol 2011;204:314.e1–11
54. Alfirevic Z, Devane D, Gyte GM. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. Cochrane Database Syst Rev 2013;5:CD006066
55. Ananth CV, Chauhan SP, Chen HY, D'Alton ME, Vintzileos AM. Electronic fetal monitoring in the United States: temporal trends and adverse perinatal outcomes. Obstet Gynecol 2013;121:927–33
56. Engle WA; American Academy of Pediatrics Committee on Fetus and Newborn. Surfactant-replacement therapy for respiratory distress in the preterm and term neonate. Pediatrics 2008;121:419–32
57. American College of Obstetricians and Gynecologists. ACOG Practice bulletin no. 106: intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. Obstet Gynecol 2009;114:192–202
58. Thangamuthu A, Russell IF, Purva M. Epidural failure rate using a standardised definition. Int J Obstet Anesth 2013;22:310–5
59. Shaikh F, Brzezinski J, Alexander S, Arzola C, Carvalho JC, Beyene J, Sung L. Ultrasound imaging for lumbar punctures and epidural catheterisations: systematic review and meta-analysis. BMJ 2013;346:f1720
60. Soens MA, Birnbach DJ, Ranasinghe JS, van Zundert A. Obstetric anesthesia for the obese and morbidly obese patient: an ounce of prevention is worth more than a pound of treatment. Acta Anaesthesiol Scand 2008;52:6–19
61. Sahota JS, Carvalho JC, Balki M, Fanning N, Arzola C. Ultrasound estimates for midline epidural punctures in the obese parturient: paramedian sagittal oblique is comparable to transverse median plane. Anesth Analg 2013;116:829–35
62. Gambling D, Berkowitz J, Farrell TR, Pue A, Shay D. A randomized controlled comparison of epidural analgesia and combined spinal-epidural analgesia in a private practice setting: pain scores during first and second stages of labor and at delivery. Anesth Analg 2013;116:636–43
63. Booth JL, Pan PH. Combined spinal epidural or traditional epidural technique: who wins? Anesth Analg 2013;116:515–6
64. George RB, Allen TK, Habib AS. Intermittent epidural bolus compared with continuous epidural infusions for labor analgesia: a systematic review and meta-analysis. Anesth Analg 2013;116:133–44
65. Sia AT, Leo S, Ocampo CE. A randomised comparison of variable-frequency automated mandatory boluses with a basal infusion for patient-controlled epidural analgesia during labour and delivery. Anaesthesia 2013;68:267–75
66. Turnbull DK, Shepherd DB. Post-dural puncture headache: pathogenesis, prevention and treatment. Br J Anaesth 2003;91:718–29
67. Basurto Ona X, Uriona Tuma SM, Martínez García L, Solà I, Bonfill Cosp X. Drug therapy for preventing post-dural puncture headache. Cochrane Database Syst Rev 2013;2:CD001792
68. Jain K, Bhardwaj N, Sharma A, Kaur J, Kumar P. A randomised comparison of the effects of low-dose spinal or general anaesthesia on umbilical cord blood gases during caesarean delivery of growth-restricted foetuses with impaired Doppler flow. Eur J Anaesthesiol 2013;30:9–15
69. Eisenach JC, Pan PH, Smiley R, Lavand'homme P, Landau R, Houle TT. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. Pain 2008;140:87–94
70. Pan PH, Tonidandel AM, Aschenbrenner CA, Houle TT, Harris LC, Eisenach JC. Predicting acute pain after cesarean delivery using three simple questions. Anesthesiology 2013;118:1170–9
71. Chooi CS, White AM, Tan SG, Dowling K, Cyna AM. Pain vs comfort scores after Caesarean section: a randomized trial. Br J Anaesth 2013;110:780–7
72. Subedi A, Biswas BK, Tripathi M, Bhattarai BK, Pokharel K. Analgesic effects of intrathecal tramadol in patients undergoing caesarean section: a randomised, double-blind study. Int J Obstet Anesth 2013;22:316–21
73. Singh SI, Rehou S, Marmai KL, Jones AP. The efficacy of 2 doses of epidural morphine for postcesarean delivery analgesia: a randomized noninferiority trial. Anesth Analg 2013;117:677–85
74. Beatty NC, Arendt KW, Niesen AD, Wittwer ED, Jacob AK. Analgesia after Cesarean delivery: a retrospective comparison of intrathecal hydromorphone and morphine. J Clin Anesth 2013;25:379–83
75. Singh S, Dhir S, Marmai K, Rehou S, Silva M, Bradbury C. Efficacy of ultrasound-guided transversus abdominis plane blocks for post-cesarean delivery analgesia: a double-blind, dose-comparison, placebo-controlled randomized trial. Int J Obstet Anesth 2013;22:188–93
76. Lee AJ, Palte HD, Chehade JM, Arheart KL, Ranasinghe JS, Penning DH. Ultrasound-guided bilateral transversus abdominis plane blocks in conjunction with intrathecal morphine for postcesarean analgesia. J Clin Anesth 2013;25:475–82
77. Griffiths JD, Le NV, Grant S, Bjorksten A, Hebbard P, Royse C. Symptomatic local anaesthetic toxicity and plasma ropivacaine concentrations after transversus abdominis plane block for Caesarean section. Br J Anaesth 2013;110:996–1000
78. Pratt SD. Anesthesia for breech presentation and multiple gestation. Clin Obstet Gynecol 2003;46:711–29
79. Carvalho B, Tan J, Macario A, El-Sayed Y, Sultan P. A cost analysis of neuroaxial anesthesia to facilitate external cephalic version for breech fetal presentation. Anesth Analg 2013;117:155–9