General Anesthesia During Pregnancy and the Postpartum Period

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Hande Gurbuz, Hulya Topcu, K. Tolga Saracoglu, and Volker Wenzel

14.1 Introduction

14.1.1 Anesthetic Considerations for Nonobstetric Surgery During Pregnancy

Hundreds of thousands of pregnant women undergo surgery for nonobstetric reasons each year. Surgery is performed on 0.75–2% of pregnant women with an indication at any gestational period for nonobstetric reasons [1]. Surgical indications for nonobstetric reasons during pregnancy include acute abdominal

H. Gurbuz (✉)
Faculty of Medicine, Department of Anaesthesiology and Reanimation, Bursa Yuksek Ihtisas Research and Training Hospital, Health Sciences University, Bursa, Turkey

Faculty of Medicine, Department of Anatomy, Kocaeli University, İzmit, Turkey
e-mail: handegrbz@gmail.com

H. Topcu
Faculty of Medicine, Department of Anaesthesiology and Reanimation, Erol Olçok Research and Training Hospital, Hitit University, Çorum, Turkey
e-mail: drtopcuh@gmail.com

K. T. Saracoglu
Faculty of Medicine, Department of Anaesthesiology and Reanimation, Lütfi Kırdar Kartal Research and Training Hospital, Health Sciences University, İstanbul, Turkey
e-mail: saracoglukt@gmail.com

V. Wenzel
Department of Anaesthesiology, Intensive Care Medicine, Emergency Medicine and Pain Therapy, Bodensee Campus Medicine, Klinikum Friedrichshafen, Friedrichshafen, Germany
e-mail: V.Wenzel@klinikum-fn.de

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diseases—appendicitis and cholecystitis—malignancies, trauma, and cardiac diseases [2–5]. Ear–nose–throat (ENT) emergencies such as epistaxis, head and neck trauma, tracheal stenosis, and cancer require surgery during pregnancy [6–12].

Surgery and anesthesia during pregnancy are critical since an intervention to the mother may also affect the baby. Anatomical, physiological, and pharmacodynamics/pharmacokinetic changes in pregnancy, limited time for preoperative anesthetic preparation due to the urgency of the intervention, and dealing with two patients at the same time are challenging even for a senior anesthesiologist. Potential risks and benefits of surgical and anesthetic interventions for a gravid patient should be taken into consideration for both mother and fetus. Thus, anesthesiologists should remodify the standard anesthetic protocols to achieve two principal goals: (1) maternal safety by having comprehensive knowledge in maternal physiology and (2) fetal safety by avoiding teratogenic agents, maintaining uteroplacental blood flow, and preventing abortion or preterm labor [13]. A multidisciplinary team of surgeons, obstetricians, anesthesiologists, and perinatologists must determine nonobstetric surgeries performed on pregnant women.

14.1.2 Timing of Surgery

The risk of abortion and preterm delivery have been predominant following nonobstetric surgeries performed during pregnancy [14]. The second trimester is considered safer for nonobstetric surgeries; however, epidemiological studies have demonstrated that the selection of the first trimester is widespread for interventions, followed by second and third trimesters [3, 4, 15]. However, when maternal hypotension and hypoxia are in control, it is suggested that the procedure performed in any period of pregnancy does not pose a higher risk to the mother and fetus than the sickness of the mother [16, 17].

Fetal mortality cannot be associated with a specific anesthetic agent or technique, but it has been suggested that the reason for surgery plays a critical role, particularly for pelvic surgeries and procedures performed for obstetric indication. In general, teratogenic effects of anesthetic agents have not been proven, but other factors such as maternal hypoxia, hypotension, vasopressor application, hypo/hypercarbia, and electrolyte disturbances remain as the major factors in teratogenicity than anesthetic agents [2]. The risk of preterm birth increases in surgeries performed in the last trimester. The timing and indications for surgery are crucial for both maternal and fetal outcomes. Thus, elective surgeries should be postponed until the postnatal period and breastfeeding. If surgery is inevitable, i.e., urgent surgeries, optimal timing is the second trimester. Only emergency surgeries should be considered during the first or the third trimester [18].

14.2 Maternal and Fetal Safety

14.2.1 Maternal Safety

14.2.1.1 Maternal Physiology and Anesthetic Implications

During pregnancy, adaptational changes affect all organ systems for the mother to tolerate pregnancy and delivery and provide maternal homeostasis as well as trigger the mother for lactation. Although hormonal fluctuations are the most responsible for changes in the first trimester, mechanical changes dominate in the second half of the pregnancy due to uterus enlargement.

Changes in the Cardiovascular System

Oxygen consumption of the cardiovascular system surges to fulfill metabolic needs of both the mother and fetus. With the mechanical pressure of the enlarged uterus in the later stages of pregnancy, the heart is shifted toward left and anteriorly. The heart expands as a consequence of blood volume increase. In echocardiographic studies, left ventricle hypertrophy occurs at the fourth gestational weeks, and the left ventricle may expand up to 50% at term [19, 20]. Dilatation occurs in the mitral, tricuspid, and pulmonary valves, but these changes are not observed in the aortic valve [21].

As of the week four of pregnancy, heart rate, stroke volume, and cardiac output increases by 20–30%, 20–50%, and 30–50%, respectively [22–24]. This elevation in cardiac output is the utmost in the first two trimesters but does not further increase in the third trimester. In the supine position, cardiac output measurements may be lower due to compression from vena cava. Escalated heart rate becomes evident in the first trimester and remains steady until the end of the pregnancy [20]. Therefore, stroke volume enlargement depends predominantly on the cardiac output increase. Ejection fraction is also heightened due to ventricular hypertrophy and dilatation [22–24], while colloid osmotic pressure decreases. In pregnant women close to term, the systemic vascular resistance and pulmonary vascular resistance reduce by 20–30%. Pulmonary artery pressure decreases slightly, but central venous pressure and pulmonary capillary wedge pressure remain unchanged [22, 23]. Postpartum measurements of these parameters return to pre-pregnancy values only in 24 weeks or longer. The perfusion of the uterus, kidneys, and extremities elevates along with an increase in the cardiac output.

Supine Hypotensive Syndrome

Gravid uterus imposes pressure on the abdominal aorta and vena cava inferior depending on the position and gestational age. The pressure on the filling of the vena cava inferior can be avoided by lifting the left lateral of the uterus by 30°. Studies have shown that vena cava inferior filling does not increase with 15° of lateral tilt position [25].

Venous return to the heart reduces drastically due to caval compression in the supine position, particularly after the 24th gestational weight. The initial response to compensate for this decrease in preload is tachycardia. If the cardiovascular system is unable to recompense in preload, bradycardia and hypotension emerge, known as the supine hypotensive syndrome. Up to 8–15% parturients experience supine hypotensive syndrome, while others are thought to maintain right atrial preload by collateral venous return [26]. The prevalent objective diagnostic criteria practiced are the reduction in the systolic blood pressure and the mean blood pressure by 15 mmHg and above, and 15–30 mmHg, respectively, concomitantly with an increase in heart rate of 20 beats/min and more.

Changes in the Respiratory System

Mucosal fragility increases due to vascular enlargement and extracellular fluid infiltration into the nasal, laryngeal, and oropharyngeal mucosa, thereby causing nasal congestion, rhinitis, or epistaxis. Airway edema can be more severe, particularly in preeclamptic pregnant women under tocolytic therapy. Besides, the difficult airway should be expected with the expansion of fat pads in the head and neck [27], thus increasing the risk of bleeding during airway manipulation. Breasts enlarge in preparation for breastfeeding but may cause difficulty in airway manipulation during intubation. Therefore, short-handled blades should be in consideration. An anesthesiologist should always be ready for potentially difficult airway in pregnant women.

In the later stages of pregnancy, due to the compression of the enlarged uterus, the vertical diameter of the chest cavity decreases by 4 cm, while the sagittal and transverse diameters expand only by 2 cm [28]. Tidal volume and alveolar ventilation also increase, accompanied by a slight rise in the breathing frequency. The net result of these changes sums up in an increase in the minute ventilation of up to 50%. Expiratory reserve volume, residual volume, and functional residual capacity diminish due to the enlarged uterus compressing the lung. However, vital capacity and total lung capacity remain consistent as a result of increased inspiratory reserve volume [29].

The closing capacity does not change in pregnant women, but a decrease in the functional residual capacity to closing capacity ratio causes smaller airways to clog faster [29]. Healthy pregnant women can tolerate this condition effortlessly, albeit it may cause hypoxemia in pregnant women with a secondary condition affecting closing capacities such as smoking, obesity, lung disease, and scoliosis.

Increased ventilation causes mild respiratory alkalosis. Arterial blood gas measurements demonstrate a decrease of $PaCO_2$ up to 30 mmHg, while PaO_2 increases to 105 mmHg [30, 31]. The acidity (pH) is stabilized by using bicarbonate buffer systems. Therefore, the $PaCO_2$ levels that are considered typical in a nonpregnant person may indicate hypercapnia for pregnant women. Adequate oxygenation for the fetus can be achieved by adjusting $PaO_2 \geq 65$ mmHg and $SpO_2 \geq 95\%$ in maternal blood. While physiological respiratory alkalosis during pregnancy shifts the oxyhemoglobin dissociation curve to the left, the maternal 2,3-diphosphoglycerate level also increases and facilitates oxygen passage to the fetus by skewing toward the left. Therefore, hyperventilation should be avoided during general anesthesia [2].

As a result of all these alterations in the lung capacity and respiratory dynamics, oxygen reserves of pregnant women diminish as well. Alveolar ventilation expansion and functional residual capacity decrease, thus accelerating intake and elimination of inhalation anesthetics. Hence, the minimal alveolar concentration (MAC) value decreases for all inhalation anesthetics in pregnant women [32]. Hypoxia develops swiftly during periods of apnea and hypoventilation, resulting in a decrease in the functional residual capacity and increased metabolic rate. By considering all these changes during pregnancy, inhalation anesthetics should be kept at lower MAC values [33]. Pre-oxygenation with 100% oxygen for 5 min is essential before general anesthesia induction.

Studies have shown that the maternal death rate due to anesthesia complications is higher with general anesthesia than with regional anesthesia for cesarean section [34]. The majority of anesthesia-related deaths occur due to airway-related problems such as aspiration, intubation difficulties, and insufficient ventilation during general anesthesia [34]. Therefore, these alarming deaths can be minimized by identifying changes in the maternal respiratory system, predicting potential complications, and taking essential precautions.

Changes in the Gastrointestinal System

Progesterone increase in pregnant women was previously associated with decreased gastrointestinal motility [35–37], but of late, it has been shown that gastric emptying time does not shorten at any period of pregnancy [38]. By contrast, gastric secretions are acidified during pregnancy, and intragastric pressure increases with the shift in the typical position of the stomach caused by the mechanical stress by the uterus. Lower esophageal sphincter tone is remarkably reduced, particularly in pregnant women with retrosternal burning. As a consequence, all pregnant women are prone to passive regurgitation, active vomiting, and pulmonary aspiration under general anesthesia. Therefore, endotracheal intubation should be performed in pregnant women undergoing general anesthesia, presuming the subject with a full stomach, and precautions should be taken into account for potential complications. Preferably, intubation should be performed with a video-assisted laryngoscope.

Other Changes

Perfusion in the skin, muscle tissue, uterus, kidney, and brain increase by cause of cardiac output and the reduction in the systemic vascular resistance during pregnancy. The half-life of neuromuscular blockers shortens in pregnant women due to increased muscle tissue perfusion. Skin temperature increase, palmar erythema, spider angioma, varicose dilatation, and hemorrhoids can also be observed as a result of vascular dilatation, angioproliferation, and congestion emerging with a direct effect of estrogen. Vasomotor instability identified by facial flushing, pallor, and Raynaud's phenomenon may be observed due to vasodilatation or vasospasm secondary to increased estrogen levels during pregnancy. Widespread nonpitting edema can be observed in the entire body, particularly in the extremities, due to the reduction in plasma oncotic pressure and capillary permeability and increased cardiac output and vena cava pressure in the later periods of pregnancy [39].

Mineralocorticoid levels increase in the plasma and total blood volume due to sodium and water retention. Physiological anemia transpires in conjunction with an increase in red blood cell volume [2]. Susceptibility to hypercoagulability and thromboembolism occurs due to increases in almost all procoagulant coagulation factors (I, VII, VIII, IX, X and XII) and fibrinogen levels [40].

Serum cholinesterase activity decreases by 20% in the term period [41], but a slight decrease in succinylcholine or ester local anesthetic (such as 2-chloroprocaine) metabolisms remains negligible. Pregnancy increases free-serum concentrations of drugs that bind to plasma proteins while hindering the albumin to globulin ratio [42]. As neural sensitivity to local anesthetics increases based upon progesterone, local anesthetic dose and concentration should be lowered in regional blocks [43, 44].

14.2.2 Fetal Safety

14.2.2.1 Fetal Effects of Anesthesia

Although in vitro and in vivo studies on fetal brain development have reported histological changes and neurodevelopmental adverse effects in the brain after exposure to most anesthetics during rapid brain development periods, there is no evidence that any specific anesthetic agent is hazardous in humans with limited exposures less than 3 h [18, 45, 46]. In 2016, the US Food and Drug Administration (FDA) issued a drug safety warning regarding the potential adverse effects of anesthetic and sedative drugs on neuronal development, especially in the third trimester of pregnancy and children under 3 years old [47]. Although human clinical studies involving young children have reported conflicting results, extensive studies indicate that a single and short anesthetic exposure does not show detrimental effects on neuronal development [48–50]. Both the FDA and the American College of Obstetrics and Gynecologists recommend not postponing inevitable surgeries during pregnancy. It is also worth noting that the cumulative dose plays a crucial role in developing congenital malformations for teratogenicity.

14.2.2.2 Fetal Effects of Maternal Factors

Healthy development of the fetus depends on sufficient oxygen intake from the placenta. Therefore, the well-being of the fetus is a function of the uteroplacental blood flow. It is obligatory to avoid hemodynamic and metabolic instabilities that cause vasoconstriction to maintain uteroplacental blood flow. In preventing hypotension, except for extreme conditions such as maternal renal failure and heart failure, a liberal fluid regimen is recommended in the perioperative period [13]. Ephedrine and phenylephrine, two vasopressor agents, can be safely used in pregnant women. The 20:1 mixture of caffeine/theodrenaline is another potent vasoactive drug that increases blood pressure by increasing cardiac output and stroke volume, without increasing the heart rate and maintaining the peripheral resistance unchanged [51]. It has a longer duration of action than ephedrine and phenylephrine, requiring less bolus administrations. There was also no significant difference

in neonatal acidosis and APGAR scores in comparison with ephedrine and phenylephrine [52].

Similar to hypotension, hypertension causes uterine artery spasms and disrupts the fetoplacental circulation. The first options in the intravenous treatment of hypertension are labetalol and hydralazine. If signs of pulmonary edema develop, nitroglycerin may be administered [53]. Maternal hypoxia and hypo/hypercapnia may also cause vasoconstriction in the uterine artery and disrupt fetal circulation [54].

14.2.2.3 Placental Transfer of Drugs

Drugs penetrate the placenta by passive diffusion. Therefore, the placental transfer is proportional to the concentration gradient on both sides of the placenta (maternal–fetal). As only free-drug fractions can pass through the placenta, the placental transfer of highly bound drugs to maternal plasma proteins is also inadequate. Most anesthetic drugs such as local anesthetics and sedatives are weak bases and have a relatively low ionization degree [44]. Neuromuscular blockers with a high degree of ionization cannot be transferred from the placenta in substantial concentrations. Nonionized drugs are more lipophilic than ionized drugs, where lipophilic drugs can penetrate tissue barriers and are more prone to traverse the placenta. Acidosis causes an increase in the ionized form of the drug. In the case of fetal acidosis, ionized drugs cannot diffuse back across the placenta, causing accumulation of the drug in the fetal plasma, known as **ion trapping** [55].

14.2.2.4 Teratogenicity

A teratogen is an agent that can disturb the intrauterine development of the embryo or fetus, producing congenital malformations. It is of consensus that teratogenesis occurs after fertilization caused by several mechanisms. Theoretically, any drug can be teratogenic if administered at a sufficiently high dose for long periods, and precisely, at the right time of the development [56, 57]. The first 2 weeks of pregnancy are an **all-or-nothing** period, meaning that exposure to teratogenic agents before organogenesis causes either the loss or intact preservation of the fetus. Moreover, exposure during the organogenesis may lead to structural abnormalities, and hence, functional problems can occur in the post-embryonic organogenesis period [58].

Although many drugs used in anesthesia have been associated with teratogenic effects in vivo, such findings are intricate to extrapolate to humans due to cross-species variation and the high dose of agents used in animal studies [45, 46]. When evaluating the likelihood of teratogenicity in maternal drug applications, the following points should be considered: (1) human teratogenicity studies cannot be performed due to ethical issues, (2) studies on experimental animals are not sufficient, and (3) use of findings to predict outcome in humans is misappropriate. Moreover, since polypharmacy is often involved during anesthesia, it is unattainable to ascribe any fetal adverse effects to only a single drug.

In many comprehensive retrospective studies, the relationship between anesthetic drugs and congenital malformations in humans has remained unknown [18]. Instead, many studies have highlighted that surgery or anesthesia is associated with preterm labor or intrauterine death, especially when administered in the first

trimester [56, 59–61]. It is thought that anesthesia complications are responsible for these adverse effects rather than the direct effects of the anesthetic drugs on the fetus [62, 63]. For instance, hypoxemia and hypotension can be teratogenic factors alone, causing physiological impairment.

In anesthesia during pregnancy, the management of risk factors in the mother as a result of physiological adaptation is crucial for the maintenance of the fetoplacental unit. Factors to consider for the fetal well-being are the needs of the growing fetus, the optimization of fetal oxygenation and uteroplacental perfusion, and both the direct and indirect impacts of the drugs. Accordingly, the anesthetic approach in nonobstetric surgery during pregnancy should be as follows:

1. Surgery should not be performed before the 16th gestational week, if possible, or at least, postponed to the second trimester.
2. The patient should be consulted with an obstetrician preoperatively.
3. Preoperative antacid administration should be considered for aspiration prophylaxis.
4. Perioperative normoxia, normocapnia, normotension, and normoglycemia should be provided.
5. Regional anesthesia should be preferred whenever possible, but nitrous oxide should be avoided if general anesthesia is preferred.
6. The fetal heart rate should be monitored before and after surgery [2].

Additionally, the use of tocolytic drugs should be discussed, and the uterus should be deviated to the left in the perioperative period, following the 16th gestational week [13, 64].

14.2.2.5 Risk Categorization of Drugs

The FDA has created a five-letter safety category for drug use in pregnancy with a system in 1979 that reviews the safety of commonly used drugs and grades the teratogenic effects of drugs (A, B, C, D, X). However, FDA implemented the Pregnancy and Lactation Labelling Final Rule, suggesting replacing the pregnancy letter categories with narrative subsections including pregnancy (labor and delivery), lactation (nursing mothers), and females and males with reproductive potential in 2015 [65, 66].

14.2.2.6 Fetal Heart Rate Monitoring

Fetal monitoring aims to detect the fetal heart rate changes that may result from maternal factors. It is recommended to document fetal heart rate before and after surgery regardless of gestational age [67, 68]. However, intraoperative fetal heart rate monitoring is challenging to interpret as there is an anticipated reduction in beat-to-beat variability under general anesthesia, and not all nonobstetric operations can be paused to allow emergency cesarean delivery. Thus, the absolute benefit to the fetus is unknown. The decision to use intermittent or continuous intraoperative fetal monitoring should be personalized based on gestational age, type of surgery, and available resources [18]. If continual fetal heart rate monitoring is selected, an

obstetrician experienced in cesarean delivery should be present to monitor and interpret the fetal heart rate throughout the surgery.

Intraoperative fetal heart rate can be monitored by an electronic fetal heart rate monitor or Doppler ultrasound. Transabdominal monitoring may be technically challenging or impractical during abdominal surgeries. In such circumstances, the use of transvaginal Doppler ultrasonography may be considered. Drugs used for general and regional anesthesia can lead to changes in the fetal heart rate. All mainstream anesthetic drugs penetrate the placenta and may result in minimal fetal heart rate variability, simultaneously with a decrease in the fetal heart rate baseline of 10–25 bpm [2]. If instantaneous unexplained fluctuations occur in fetal heart rate, it is mandatory to evaluate the maternal condition to unravel the factors causing interruption of the uteroplacental blood flow. The objective of the optimization of the maternal condition is to improve the impaired uteroplacental blood flow. Parameters to consider for optimization are to increase left uterine displacement, to correct oxygenation and acid-base status, to treat hypotension, to ensure appropriate end-tidal CO_2 and hemoglobin levels, to check the surgical site to rule out any external compression impairing the uteroplacental perfusion, and to consider the administration of drugs to improve uterine relaxation (i.e., volatile agents, nitroglycerin) [2].

14.2.2.7 Avoidance and Treatment of Preterm Delivery

The incidence of spontaneous abortion, premature birth, and preterm delivery after nonobstetric surgery during pregnancy has increased due to surgery itself, manipulation of the uterus during surgery, and maternal systemic disease (i.e., infection) [69]. The risk of miscarriage during pregnancy is higher in the first and third trimesters. Routine prophylactic tocolytic application is controversial. However, in acute preterm labor, intravenous hydration, calcium channel blocking agents, cyclooxygenase inhibitors (NSAID), beta-mimetics, and magnesium sulfate can be given in agreement with an obstetrician's decision [54]. Antenatal corticosteroid administration should be considered for fetal lung maturation.

14.3 Anesthetic Drugs

14.3.1 Frequently Used Drugs for Anesthesia and Analgesia

14.3.1.1 Benzodiazepines

Benzodiazepines are often used during pregnancy to manage severe anxiety or agitation, or drugs with the shortest half-lives such as lorazepam and midazolam are of consideration. Some studies suggest that long-term use of benzodiazepines in early pregnancy is associated with cleft palate and congenital inguinal hernia [70, 71]. A single exposure to benzodiazepines in pregnant women for perioperative or operative purposes does not cause congenital malformations. It is further stated that benzodiazepines can be beneficial for the fetus by controlling the catecholamine level arising from preoperative surgical stress [72]. In postpartum use, benzodiazepines are transmitted to milk because of their lipophilic nature. Therefore, the utmost

caution should be exercised in chronic use during the lactation period, and the administration doses should be adjusted accordingly.

14.3.1.2 Opioids

Opioids are commonly used in anesthesia to reduce the response to laryngoscopy and for analgesia. Opioids—highly lipophilic and low-molecular-weight drugs—easily egress the placenta. While the known maternal side effects of systemic opioids are sedation, respiratory depression, postural hypotension, constipation, delayed gastric emptying, bradycardia, and cardiac arrest, opioids in the placenta infiltrating into the fetus may cause respiratory depression and changes in the fetal heart rate [18]. Opioid elimination in newborns and fetuses is more prolonged than in adults. Although opioids used in general anesthesia are more likely to cause respiratory depression in the newborn, a meta-analysis of the use of opioids (alfentanil, remifentanil, and fentanyl) for the induction of cesarean delivery did not show a significant difference in the first- and fifth-minute APGAR scores post-opioid administration [73]. Opioids used in regional anesthesia have less maternal and fetal-neonatal side effects than their systemic use [74]. The long-term use of opioids during pregnancy for either medical reasons or drug addiction can cause neonatal opioid withdrawal syndrome that could be life-threatening [75, 76]. Several studies have shown that opioids may be associated with congenital disabilities, including neural tube defects, congenital heart defects, gastroschisis, or weak fetal growth, stillbirth, and premature birth due to chronic maternal use [77].

Morphine is a potent opioid with high μ-opioid receptor affinity with a longer half-life. UGT2B7 metabolizes morphine to morphine-3-glucuronide (70%) and morphine-6-glucuronide (M6G; 30%) in the liver [78]. M6G is an active metabolite and 13 times more potent than morphine. By rapidly egressing the placenta, drug levels in fetal blood in the fifth minute escalate to a value closer to the maternal serum levels [79]. Since the liver is immature in newborns, the half-life of M6G is longer in infants than in adults. Morphine causes respiratory depression predominantly in newborns due to the high brain permeability. Due to the altered pharmacodynamics and pharmacokinetics during pregnancy, the plasma clearance of morphine increases, and the half-life is shortened compared to nonpregnant women. Theoretically, these changes are expected to reduce fetal exposure. Morphine and its metabolites egress into breast milk in trace amounts. Detrimental effects are not expected in a single application, but the newborn should be monitored closely for a latent respiratory depression in repetitive usage.

Meperidine (pethidine) is a synthetic opioid that agonistically affects through μ- and κ-opioid receptors. It has a potency of 10% of morphine with a half-life of 2.5–3 h. Meperidine is metabolized to normeperidine in the liver, causing convulsions with a prolonged activity period (14–21 h) [79]. It reaches the balance in maternal and fetal blood by passing through the placenta due to its high liposolubility. It can be used as a single dose in the perinatal period and lactation. However, it is not recommended during lactation since it causes accumulation of normeperidine in infants with repeated use [80].

Fentanyl is a highly liposoluble and protein-bound synthetic opioid that binds to μ-opioid receptors. It is metabolized in the liver to inactive metabolites via CYP3A. It has a fast release and short duration of action, thus causing less neonatal respiratory depression than meperidine. Its single use is considered safe during breastfeeding, but there is insufficient data on its continual use [79, 81].

Alfentanil and sufentanil are potent synthetic mu-opioid receptor agonist analgesic drugs. Alfentanil is an analog of fentanyl that is only 10% potent but has a shorter duration of action and quicker onset. Available data on pregnant women are insufficient to relate the drug with birth defects and miscarriage. Sufentanil is ten times as potent as fentanyl. It has a half-life shorter than fentanyl but longer than alfentanil.

Remifentanil is a selective μ-opioid receptor agonist with a rapid onset of action and a very short half-life, as low as 3–10 min. The placental transfer is very low due to its rapid hydrolysis by nonspecific tissue and plasma cholinesterases. It is considered to be appropriate for use in anesthesia for surgical interventions during pregnancy and the peripartum period. However, one should not underestimate that it may impair uteroplacental circulation due to hypotension. Mothers administered with remifentanil should be closely monitored for respiratory depression [82].

Tramadol is a weak μ-opioid receptor agonist metabolized in the liver by demethylation and glucuronidation through CYP2D6 (codeine is also metabolized by CYP2D6) to its active metabolite *O*-desmethyl tramadol. Tramadol hinders the central neuronal reuptake of serotonin and norepinephrine. Analgesic potency of tramadol is comparable to meperidine, and 10–20% of morphine, causing less respiratory depression than morphine in analgesic doses equal to morphine [79]. Both tramadol and its metabolite *O*-desmethyl tramadol are excreted into breastmilk [83]. Similar to codeine, there are clinically critical consequences of tramadol metabolism via the cytochrome P450 isoenzyme CYP2D6. CYP2D6 has a considerable genetic polymorphism whose function is deficient in poor metabolizers, while relatively higher in ultra-rapid metabolizers [84]. The clinical reflection of this diversity is that the efficacy and side effects of the drug are low in poor metabolizers but are higher in ultra-rapid metabolizers. In ultra-rapid metabolizers, the drug passes into breast milk in substantial amounts. Prediction of both maternal and neonatal effects of tramadol and codeine is impractical since the type of CYP2D6 genotype is unknown in patients. Case reports of severe neonatal respiratory depression and even deaths due to tramadol use have been reported in the literature [81, 84]. Thus, the use of tramadol is not recommended during breastfeeding [85]. In some countries, the use of tramadol in children under 12 is prohibited.

14.3.1.3 Hypnotics

Propofol enables rapid and smooth induction of anesthesia with a short duration of action and fast recovery time. It effectively controls the cardiovascular response to laryngoscopy. Propofol also has an anti-emetic activity but not an analgesic effect. It is popular in a wide range of uses in general anesthesia and sedation. However, propofol may interfere with uteroplacental blood flow that ultimately causes

cardiovascular depression and hypotension in a dose-dependent manner. Also, propofol is a nonionized and highly liposoluble anesthetic agent that can penetrate through the placenta [72]. It can be detected in breast milk in trace amounts since it is rapidly cleansed from the plasma.

Thiopentone is a barbiturate with neuroprotective and anticonvulsant effects and is favored in rapid serial induction for its rapid-onset characteristic. It has a longer context-sensitive half-life in comparison with propofol. Barbiturates have no analgesic effect but are associated with postoperative barbiturate-hyperalgesia. Thiopentone decreases cardiac output and causes hemodynamic instability and respiratory depression in a dose-dependent fashion; altogether, it may adversely affect uteroplacental blood flow.

It has high lipid solubility with affinity to plasma proteins and rapidly passes from the placenta to the fetus. It reaches the maximum dose approximately within a minute in the umbilical cord vein. It passes through the placenta immediately after anesthesia induction, but its effect is observed in the fetus within 45 s. After 2–3 min, thiopental concentrations in the maternal and fetal blood balance, and the drug concentration moderately decreases in both. The drug infiltrates into the fetal brain tissue, but the dose of thiopental lesser than 4 mg/kg in induction does not cause fetal depression, thus considered safe in obstetric patients [72].

Ketamine is an NMDA blocker used for anesthesia induction and sedation. Unlike propofol and thiopentone, ketamine has analgesic properties. It may be selected in asthmatic patients due to its bronchodilator effect but is not suitable for use in hypertensive patients due to its sympathomimetic activity. Relative hemodynamic stability makes ketamine a preferred agent for many emergency cases [86]. Ketamine is more liposoluble and less protein-bound than thiopental, so it rapidly passes through the placenta and saturates in the fetus 1–2 min after maternal administration. It increases uterine tone at doses above 1 mg/kg; hence, the dosage should be kept below 1 mg/kg when it is administered in pregnant women [72]. Ketamine is associated with awareness during anesthesia. Also, it can cause the emergence of delirium and hallucinations. These adverse effects can be prevented by administering benzodiazepines or barbiturates simultaneously.

Etomidate, a GABA-A agonist, is usually preferred for its safe hemodynamic profile. However, it can lead to nausea and vomiting, hiccups, myoclonus, and pain at the injection site. Moreover, it causes adrenal suppression in long-term use and lowers the seizure threshold. It can also cause adrenal suppression in the neonate and decrease the cortisol levels after maternal anesthesia induction. Therefore, etomidate use in obstetric patients is not recommended [87].

14.3.1.4 Volatile Anesthetics

MAC values of the inhalation agents used in anesthesia decrease due to the physiological changes during pregnancy. Therefore, providing adequate anesthesia with low-dose inhalation anesthesia reduces the depressive effects in infants.

Sevoflurane, desflurane, and isoflurane are commonly used in volatile anesthetics nowadays. No teratogenicity effect has been reported with the use of volatile anesthetics during pregnancy [57]. A critical disadvantage of volatile anesthetics is

that they increase postpartum blood loss by decreasing uterine muscle tone in a dose-dependent manner. These effects can be reduced by using low concentrations with administrating oxytocin concomitantly.

Nitrous oxide is a low-molecular-weight and nonlipophilic molecule. It diffuses through the placenta depending on the exposure time but does not affect uterine contractions and fetal heart rate. Nitrous oxide causes the oxidation of vitamin B12 and prevents the activation of methionine synthase. Methionine synthase is an essential enzyme for DNA synthesis. Therefore, it should be avoided in the first trimester of pregnancy. Its use is not recommended because there are opioid alternatives to substitute its usage as an analgesic in early pregnancy. No adverse event has been reported due to its use in the later periods of pregnancy. Nitrous oxide is also widely used as an inhalational agent in labor analgesia [88].

14.3.1.5 Neuromuscular Blockers

Muscle relaxants are used to facilitate endotracheal intubation and to increase surgical comfort. Neuromuscular blocking agents have a polar molecular structure and cannot pass through the placenta; thus, no fetal adverse effects have been reported. Their metabolism may be affected depending on the physiological changes during pregnancy. No adverse effects in the infant have been reported as the transition of the drug into milk during the postpartum period is negligible.

Succinylcholine is a hydro-soluble depolarizing muscle relaxant. For this reason, the amount of the drug passed into the fetus is negligible and does not cause neonatal respiratory depression. Suitable conditions for intubation occur within 45 s after intravenous administration, and the drug is eliminated from the body by plasma cholinesterases. Plasma cholinesterase levels decrease by about 25% from the beginning of pregnancy until the postpartum 7 days [89].

Rocuronium has substituted succinylcholine due to its rapid onset of action. After introducing sugammadex, the relaxant binding agent selective for rocuronium and vecuronium, rocuronium becomes a non-depolarizing muscle relaxant in difficult airway management of choice. A regular dose of rocuronium is 0.6 mg/kg, and while it provides the suitable conditions for intubation in about 98 s, intubation can be achieved within 60 s by increasing the induction dose up to 1–1.2 mg/kg. The placental transfer of rocuronium is negligible. Having the least placental transfer among the neuromuscular blocking agents, rocuronium has become widespread for obstetric anesthesia [90].

Vecuronium is another non-depolarizing muscle relaxant that is not preferred in pregnant women due to its long onset time and prolonged duration of action [90].

Atracurium and cis-atracurium are neuromuscular blocking agents that undergo organ-independent elimination (Hoffman degradation). They may cause histamine discharge and hypotension in high doses for rapid onset. These muscle relaxants are not recommended in pregnant women as hypotension may cause fetal adverse effects with decreased uteroplacental blood flow. However, organ-independent elimination is a suitable option for repeated doses of muscle relaxants in pregnant women with liver or renal dysfunction [90].

14.3.1.6 Neuromuscular Block Reversal Agents

Neostigmine is a cholinesterase inhibitor used for the reversal of non-depolarizing muscle relaxants. Neostigmine is administered simultaneously with sympathomimetics such as atropine or glycopyrrolate to oppose its parasympathomimetic effects. It passes through the placenta in trace amounts. When combined with glycopyrrolate, fetal bradycardia may occur since the dosage of glycopyrrolate passing out the placenta is lower than neostigmine. Thus, neostigmine is recommended for use in conjunction with atropine [91].

Sugammadex is a gamma-cyclodextrin that inactivates steroid neuromuscular blocking agents by encapsulation. The dose of sugammadex depends on the level of neuromuscular blockade with the highest affinity for rocuronium, followed by vecuronium, pancuronium, and pipecuronium, respectively [92].

Sugammadex has several clinical advantages over neostigmine. However, sugammadex also diminishes free progesterone levels by binding progesterone with encapsulation. This effect may be significant, as progesterone is required for endometrial decidualization and uterine growth in the early pregnancy and is crucial for the maintenance of pregnancy. It is known that administration of anti-progesterone drugs such as onapristone or mifepristone results in miscarriage or preterm labor [93]. Therefore, the use of sugammadex in pregnant women, except for the cesarean section in the third trimester, has raised serious concerns due to progesterone interaction. Although in vivo studies have shown that sugammadex administration during the first trimester of pregnancy does not result in any fetal risk, there are no case reports or studies in humans [94]. Besides, sugammadex interacts with progesterone containing oral contraceptives, reducing the efficacy of the drug. Hence, a nonhormonal contraception method should be reconsidered for the following 7 days after sugammadex administration [95].

14.3.1.7 Anticholinergic Drugs

Atropine is an anticholinergic agent commonly used perioperatively for its antisialagogue and anti-asthmatic properties, constituting the first-line treatment in suppressing parasympathetic activation and treatment of life-threatening bradycardic rhythms and poisonings (i.e., organophosphate pesticides). Atropine passes the placenta, causing fetal tachycardia [91]. Although the use of atropine during pregnancy has not been shown to cause any teratogenicity, its safety has been uncorroborated. Therefore, it should only be used in cases when there is no other alternative. Atropine is excreted into milk and may cause anticholinergic effects in infants. Also, having been shown to inhibit lactation, its usage should be avoided for breastfeeding women unless indispensable [96].

Glycopyrrolate is a synthetic anticholinergic drug used perioperatively for the same indications with atropine. Because glycopyrrolate cannot cross the blood–brain barrier, it is less likely to cause altered mental status than atropine. Glycopyrrolate does not cross the placenta, and it does not excrete into breastmilk [97].

14.3.1.8 Nonopioid Analgesics

Nonopioid analgesics are used to avoid the unforeseen adverse effects of opioid analgesics.

Paracetamol is an analgesic used widespread during pregnancy. It can be used safely in the treatment of mild to moderate pain at any stage of pregnancy. However, in some studies, it has been argued that the maternal use of paracetamol in recurrent doses may be associated with neonatal asthma and neurobehavioral problems [98–100]. Paracetamol is considered to be safe to use during the lactation period. Although it passes into breastmilk at varying amounts, the dose of paracetamol uptaken by the baby with milk is lower than the therapeutic range [81].

Nonsteroidal anti-inflammatory drugs are associated with premature closure of fetal ductus arteriosus and oligohydramnios; thus, their use during pregnancy is generally contraindicated unless inevitable. For example, in some specific cases such as preeclampsia, antenatal low-dose aspirin use is recommended [101]. It has also been stated that ibuprofen, diclofenac, naproxen, celecoxib, ketorolac, and low-dose aspirin (not in analgesic doses) are compatible with breastfeeding during the lactation period [81].

14.4 Anesthesia Management

14.4.1 General Anesthesia

Although both regional and general anesthesia can be safely applied for operations performed for nonobstetric reasons during pregnancy, it is recommended to prefer regional techniques whenever possible [58, 72]. The type of anesthesia should be chosen according to the maternal and fetal conditions, indications, location, and the duration of surgery.

14.4.1.1 Preanesthetic Evaluation

The pregnancy status of the patients at childbearing age is not routinely checked before surgery. The ASA Practice Advisory for Preanesthesia Evaluation recommended that pregnancy testing may be offered to the patients, especially before the procedures that are expected to expose the fetus to potential teratogens [102–104].

Standard preoperative assessment should be held with meticulous attention to the airway. The mother should be informed about potential teratogenicity and difficult airway. The patient should be consulted preoperatively with an obstetrician and perinatologist. Also, a pediatrician should be involved in the team if preterm delivery is anticipated.

Verbal reassurance is preferred over pharmacologic premedication. Gastric emptying in pregnant women is comparable to nonpregnant patients [105]. However, antacid prophylaxis is required after 14 weeks of gestation [106]. A combination of nonparticulate antacids and H2-receptor blockers is sufficient to increase the gastric pH. Ultrasound assessment of gastric content can be used to individualize the risk

of tracheal aspiration [107]. Besides, the prophylaxis of venous thromboembolism should be considered.

14.4.1.2 Rapid Sequence Induction and Intubation

Rapid sequence induction and intubation (RSII) for anesthesia is a technique designed to minimize the possibility of pulmonary aspiration in patients at risk by placing an endotracheal tube as quickly as possible after induction. The RSII is generally used in emergency services and procedures. Indications for RSII include patients with a full stomach, gastrointestinal physiological changes, increased abdominal pressure, and pregnancy after 20 weeks of gestation with increased aspiration risk with anesthesia induction.

Before RSII, a thorough airway evaluation is required. Not in all but the most urgent cases, a rapid airway assessment and questioning of previous airway problems should be conducted. If difficult airway management is anticipated, a modified RSII with awake intubation may alternatively be chosen.

The preparation of equipment for RSII should be similar to routine induction. Standard and alternative airway devices should be readily available, including small, medium, and large face masks, various sizes and types of laryngoscopes, oral and nasal airways, several sizes of supraglottic airways, and a bougie, which should be of reach. Alternative laryngoscopy devices, including video laryngoscopes and flexible bronchoscopes, and other emergency airway and aspiration apparatus should be available and quickly accessible.

Anxiolytics may be administered if the patient is hemodynamically stable. Generally, prokinetics and antacids can be administered before the procedure. Due to physiological changes in pregnant women, all patients should be pre-oxygenated with 10 L/min 100% oxygen before general anesthesia to increase oxygen reserve and provide additional time to secure the airway. Pre-oxygenation is particularly crucial before RSII, as the mask ventilation with this technique is usually not carried out between induction and intubation periods [108]. Immediately post-induction, cricoid pressure is recommended until the patient is intubated [109, 110]. However, the use of cricoid pressure is controversial as it may lead the airway more difficult when misapplied, and its efficacy in preventing pulmonary aspiration may be insufficient [111]. The patient is given an appropriate hypnotic agent, often thiopental and most often propofol, and a neuromuscular blocker, especially in pregnant women. The first choice is to inject succinylcholine (or high-dose rocuronium) intravenously and to make it suitable for intubation within approximately 45–60 s. The endotracheal cuff is inflated immediately following intubation.

Possible complications of RSII include the inability to intubate, hypoxemia, hypotension, and pulmonary aspiration, all of which have adverse effects on pregnant women and fetuses. Therefore, it may be worthwhile to determine the cricothyroid membrane position by palpating the cricothyroid membrane during pre-oxygenation since front-of-neck access is required in a possible failed intubation. Also, the use of ultrasound may help monitor the cricothyroid membrane [112, 113].

Airway complications and pulmonary aspiration can occur while emerging from anesthesia. In most cases, an orogastric or nasogastric tube should be put in during anesthesia to drain the gastric content by aspirating.

Patients should be kept intubated with the endotracheal tube cuff inflated until the airway reflexes are fully restored. It would be helpful to extubate obstetric patients in the left lateral or head-up position [110]. Patients should be transferred to the post-anesthesia care unit in a head-up position to reduce the possibility of regurgitation [114].

14.4.1.3 Difficult Airway Management

Difficult airway should always be expected due to physiological changes in pregnant women. If general anesthesia is required in patients with difficult airway anticipation, the procedure should be started with all the equipment and an experienced team for difficult airway management.

An experienced anesthesiologist should perform intubation due to the risk of pulmonary aspiration, difficult airway, and inadequate ventilation depending on physiological changes of pregnant women. Before the induction, the pregnant patient should be pre-oxygenated with 10 L/min 100% oxygen [109]. Short handled blades can be preferred to ease the manipulation of laryngoscopes because of the enlarged breasts. Multiple intubation attempts pose a risk for complications; therefore, successful intubation at the first attempt should be the priority [115]. No more than two attempts should be made with direct laryngoscopy because of airway difficulty increases due to the risk of bleeding and edema after each attempt [110]. Although video laryngoscopy provides excellent advantages, it should be discontinued after two unsuccessful attempts, but instead, supraglottic airway devices such as laryngeal masks should be considered [109, 116]. In the case of two failed attempts in the placement of supraglottic airway devices, the necessary procedures for invasive airway access (front-of neck access or surgical cricothyrotomy) should be applied immediately [109, 110].

Cannot Intubate–Cannot Ventilate

If the patient cannot be ventilated with a face mask or supraglottic airway devices, front-of neck access or surgical cricothyrotomy should be performed immediately. If the maternal condition deteriorates and cardiac arrest develops, maternal advanced life support should be started immediately, and perimortem cesarean delivery should be considered in pregnant women over 20 gestational weeks [110].

14.5 Anesthesia and Postoperative Analgesia in Lactation

During lactation, the breastfeeding mother may need anesthesia or analgesic medication. However, there are some concerns about using anesthetic or analgesic drugs during lactation due to potential harm to the infants by drug-tainted milk. The effect of drugs on the infant may vary depending on various factors such as the type of

drugs, the amount of maternal exposure, the breastfeeding period, and the amount of milk. However, studies on this subject are limited.

Drugs contaminate breast milk through intracellular junctions between lactocytes. Intracellular junctions of lactocytes start narrowing 24–48 h after birth and are fully sealed on postpartum 7–10 days [81]. Since the amount of colostrum in the first 24–48 h in the postpartum period is meager, the transmission of maternally administered drugs to the newborn in the early postpartum period is deficient [117]. However, when the amount of milk increases in later periods, the transition of drugs to the infant would also increase. Hence, the exposure of the newborn to maternally administered drugs culminates between the postpartum third and tenth days [81].

As a thumb rule for systemic drug applications during the lactation period, it is recommended to use anesthetic and analgesic drugs at minimal doses as the drugs may pass into breast milk in incalculable amounts [118]. Multimodal analgesia methods are strongly recommended for reducing drug doses in treating maternal pain. In postoperative analgesia, nonsteroidal anti-inflammatory drugs, opioids, and nerve blocks can be used alone or in combination. Locoregional anesthesia and analgesia techniques should be considered part of the multimodal regimen in postoperative pain control during lactation and pregnancy. In some cases, for instance, ENT surgeries, regional anesthesia would provide adequate pain control without the need for additional systemic medication. The first-line systemic analgesic should be nonopioid analgesics in treating maternal pain. In the case of opioids usage, their use should be limited to a minimal effective dose momentarily [117].

Anesthetic drugs having extremely short half-life are rapidly redistributed in the body. For short-term interventions, it is suggested that the mother can start breastfeeding immediately after surgery, but not to pump and dump the milk [81]. It is also essential to monitor the alertness of both the mother and the baby attentively. When the mother receives high doses of medication, discarding the breastmilk for 24–48 h prevents the exposure of the infant to drugs. However, given that the drugs are excreted in breast milk in relatively lower amounts from the systemic circulation, and milk goes into the stomach, not intravenous, breastfeeding can still be continued if the benefits outweigh the risks [117].

14.6 Cardiopulmonary Resuscitation in Pregnancy

Cardiac arrest during pregnancy is infrequent and limited in merely case reports/series. Nonetheless, according to the data available, maternal survival is lower than in other reported epidemiological studies [119, 120]. Cardiopulmonary resuscitation (CPR) in pregnancy is complicated because the mother and fetus are affected concomitantly. Therefore, precautions should be taken for both maternal cardiac arrest and neonatal resuscitation. Besides, when perimortem cesarean delivery is required, the management of these patients requires multidisciplinary team collaboration. While applying basic and advanced cardiac life support algorithms in pregnant women, these protocols should be remodified depending on physiological and anatomical changes during the pregnancy. The resuscitation team should be aware of physiological changes in the pregnancy that may affect resuscitation techniques.

14.6.1 Differences in Basic Life Support and Advanced Cardiovascular Life Support in Pregnant Women

14.6.1.1 Basic Life Support

Pregnant women are more disadvantageous in respiration and hemodynamics than nonpregnant adults depending on the physiology of pregnancy. Also, they are more vulnerable to develop hypoxemia rapidly with apnea due to limited oxygen reserves with increased metabolism. When the uterus is at or above the umbilicus level, pregnant women tend to instigate hypotension due to aortocaval compression when lying in the supine position. In such cases, basic life support (BLS) should be applied immediately. While evaluating the responsiveness of the patient, the location of the uterus should also be spotted promptly with reference to the umbilicus level. Simultaneous **U**terine displacement should also be added to the **C**irculation-**A**irway-**B**reathing assessment (i.e., C-A-B-U) [121–123]. All these tasks must be executed concurrently, not sequentially. The BLS requires a minimum of four responders to be present [123].

14.6.1.2 Circulation

As in all adult CPRs, high-quality chest compressions should be performed at a rate of at least 100 per minute at a depth of at least 5 cm allowing full recoil, and at a compression ventilation ratio of 30:2 with minimal interruptions. Manual uterine displacement should be performed by another rescuer to prevent aortocaval compression. For effective and high-quality chest compressions, the patient should be in the supine position, not left lateral tilt [124, 125]. Previous guidelines have suggested positioning the hands slightly above the sternum for chest compressions in CPR in pregnancy, but the evidence is not convincing. Thus, hands should be positioned in the middle of the chest and lower half of the sternum in pregnant women with chest compressions as in nonpregnant adults. Defibrillation protocol is identical to that of nonpregnant adults since the transthoracic impedance does not change [123]. Fetal monitoring is not recommended during CPR to avoid interruption of cardiac compressions. However, if delivery is still not achieved after a successful CPR, fetal heart rate can be monitored for fetal evaluation.

14.6.1.3 Airway

Airway management should always be considered problematic in pregnant women due to airway edema and obesity. Pregnant women are at risk of the rapid development of hypoxemia as a result of decreased functional residual capacity and increased oxygen consumption and increased intrapulmonary shunt. Early two-handed (not a single-handed technique) bag-mask ventilation with a 100% oxygen of 15 L/min while avoiding hyperventilation is crucial to prevent desaturation in a pregnant woman. Because of the risk of a difficult airway, intubation should be performed by an experienced laryngoscopist [126]. Alternative airway interventions such as supraglottic airway devices or cricothyrotomy should be considered after two unsuccessful laryngoscopy attempts [108, 127–130]. The cricoid pressure—Sellick maneuver—to prevent vomiting during intubation has not been effective [111, 131]. It also renders intubation attempts more difficult, thus not recommended

during CPR [132]. If the fundus of the uterus is at or above the umbilicus level, a lower tidal volume should be applied compared to levels in nonpregnant women.

14.6.1.4 Perimortem Cesarean Delivery

If there is no response to CPR within 4 min, emergency perimortem cesarean delivery should be planned in pregnant women with a uterus extending to or above the umbilicus level regardless of the gestational age and fetal viability [133]. An emergency hysterotomy is not essential in all pregnant women but life-saving for the mother whose cardiac arrest is thought to be due to aortocaval compression [134, 135].

14.6.1.5 Drugs Used During Advanced Cardiovascular Life Support

All of the drugs used during CPR in nonpregnant adults are also recommended in the same dose for CPR in pregnant women. The lower extremity should not be preferred for intravenous access because the blood return to the heart is impaired due to caval pressure. In cases where intravenous access is not possible, the intraosseous route should be considered.

If hypovolemia or bleeding is considered a possible cause of cardiac arrest during pregnancy, fluid resuscitation and blood product replacement should be performed immediately.

If the patient is being infused with magnesium in the prearrest period and magnesium intoxication is considered a cause of cardiac arrest, magnesium infusion should be discontinued, and then calcium chloride (10 mL) or calcium gluconate (30 mL) should be given intravenously [136].

Regional anesthesia is the primary recommended method of anesthesia for patients during pregnancy. If local anesthetic systemic toxicity (LAST) is considered the cause of cardiac arrest, the LAST protocol should be conducted immediately (see: Chap. 13: Locoregional Anaesthesia During Pregnancy and the Post-partum Period).

References

1. Reitman E, Flood P. Anaesthetic considerations for non-obstetric surgery during pregnancy. Br J Anaesth. 2011;107:72–8.
2. Bauchat JR, van de Velde M. Nonobstetric surgery during pregnancy. In: Chestnut DH, editor. Chestnut's obstetric anesthesia: principles and practice. 6th ed. Philadelphia: Elsevier; 2019.
3. Devroe S, Bleeser T, van de Velde M, et al. Anesthesia for non-obstetric surgery during pregnancy in a tertiary referral center: a 16-year retrospective, matched case-control, cohort study. Int J Obstet Anesth. 2019;39:74–81.
4. Vujic J, Marsoner K, Lipp-Pump AH, et al. Non-obstetric surgery during pregnancy—an eleven-year retrospective analysis. BMC Pregnancy Childbirth. 2019;19:382. https://doi.org/10.1186/s12884-019-2554-6.
5. Arkenbosch JHC, van Ruler O, de Vries AC. Non-obstetric surgery in pregnancy (including bowel surgery and gallbladder surgery). Best Pract Res Clin Gastroenterol. 2020;44–45:101669. https://doi.org/10.1016/j.bpg.2020.101669.

6. Kastrinidis N, Kleinjung T. Blocked nose, nosebleeds, ringing in the ear: ENT diseases during pregnancy. Praxis (Bern 1994). 2019;108:329–34.
7. Lippincott LH, Amedee RG. ENT issues in pregnancy. J La State Med Soc. 1999;151:350–4.
8. Vlastarakos PV, Manolopoulos L, Ferekidis E, et al. Treating common problems of the nose and throat in pregnancy: what is safe? Eur Arch Otorhinolaryngol. 2008;265:499–508.
9. Kumar R, Hayhurst KL, Robson AK. Ear, nose, and throat manifestations during pregnancy. Otolaryngol Head Neck Surg. 2011;145:188–98.
10. Cornthwaite K, Varadharajan K, Oyarzabal M, et al. Management of prolonged epistaxis in pregnancy: case report. J Laryngol Otol. 2013;127:811–3.
11. Kiciński K, Skorek A, Stankiewicz C. Managment of head and neck cancers during pregnancy. Otolaryngol Pol. 2011;65:326–32.
12. Scholz A, Srinivas K, Stacey MRW, et al. Subglottic stenosis in pregnancy. Br J Anaesth. 2008;100:385–8.
13. Upadya M, Saneesh PJ. Anaesthesia for non-obstetric surgery during pregnancy. Indian J Anaesth. 2016;60:234–41.
14. Mazze RI, Källén B. Appendectomy during pregnancy: a Swedish registry study of 778 cases. Obstet Gynecol. 1991;77:835–40.
15. Mazze RI, Källén B. Reproductive outcome after anesthesia and operation during pregnancy: a registry study of 5405 cases. Am J Obstet Gynecol. 1989;161:1178–85.
16. Tolcher MC, Fisher WE, Clark SL. Nonobstetric surgery during pregnancy. Obstet Gynecol. 2018;132:395–403.
17. Balinskaite V, Bottle A, Sodhi V, et al. The risk of adverse pregnancy outcomes following nonobstetric surgery during pregnancy: estimates from a retrospective cohort study of 6.5 million pregnancies. Ann Surg. 2017;266:260–6.
18. American College of Obstetricians and Gynecologists and American Society of Anesthesiologists. ACOG Committee Opinion No. 775: nonobstetric surgery during pregnancy (interim update). Obstet Gynecol. 2019;133:285–6.
19. Schannwell CM, Zimmermann T, Schneppenheim M, et al. Left ventricular hypertrophy and diastolic dysfunction in healthy pregnant women. Cardiology. 2002;97:73–8.
20. Robson SC, Hunter S, Boys RJ, et al. Serial study of factors influencing changes in cardiac output during human pregnancy. Am J Phys. 1989;256:1060–5.
21. Campos O, Andrade JL, Bocanegra J, et al. Physiologic multivalvular regurgitation during pregnancy: a longitudinal doppler echocardiographic study. Int J Cardiol. 1993;40:265–72.
22. Abbas AE, Lester SJ, Connolly H. Pregnancy and the cardiovascular system. Int J Cardiol. 2005;98:179–89.
23. Fujitani S, Baldisseri MR. Hemodynamic assessment in a pregnant and peripartum patient. Crit Care Med. 2005;33:354–61.
24. Desai DK, Moodley J, Naidoo DP. Echocardiographic assessment of cardiovascular hemodynamics in normal pregnancy. Obstet Gynecol. 2004;104:20–9.
25. Higuchi H, Takagi S, Zhang K, et al. Effect of lateral tilt angle on the volume of the abdominal aorta and inferior vena cava in pregnant and nonpregnant women determined by magnetic resonance imaging. Anesthesiology. 2015;122:286–93.
26. Lanni SM, Tillinghast J, Silver HM. Hemodynamic changes and baroreflex gain in the supine hypotensive syndrome. Am J Obstet Gynecol. 2002;187:1636–41.
27. Pilkington S, Carli F, Dakin MJ, et al. Increase in Mallampati score during pregnancy. Br J Anaesth. 1995;74:638–42.
28. Crapo RO. Cardiopulmonary physiology during pregnancy. Clin Obstet Gynecol. 1996;39:3–16.
29. Kolarzyk E, Szot WM, Lyszczarz J. Lung function and breathing regulation parameters during pregnancy. Arch Gynecol Obstet. 2005;272:53–8.
30. Shankar KB, Moseley H, Vemula V, et al. Arterial to end-tidal carbon dioxide tension difference during anaesthesia in early pregnancy. Can J Anaesth. 1989;36:124–7.
31. Templeton A, Kelman GR. Maternal blood-gases, (PAO2-PaO2), physiological shunt and vd/vt in normal pregnancy. Br J Anaesth. 1976;48:1001–4.

32. Goodman S. Anesthesia for nonobstetric surgery in the pregnant patient. Semin Perinatol. 2002;26:136–45.
33. Fanzago E. Anaesthesia for non obstetric surgery in pregnant patients. Minerva Anestesiol. 2003;69:416–27.
34. Hawkins JL, Koonin LM, Palmer SK, et al. Anesthesia related deaths during obstetric delivery in the United States, 1979-1990. Anesthesiology. 1997;86:277–84.
35. Levy DM, Williams OA, Magides AD, et al. Gastric emptying is delayed at 8-12 weeks' gestation. Br J Anaesth. 1994;73:237–8.
36. Lawson M, Kern F Jr, Everson GT. Gastrointestinal transit time in human pregnancy: prolongation in the second and third trimesters followed by postpartum normalization. Gastroenterology. 1985;89:996–9.
37. Chiloiro M, Darconza G, Piccioli E, et al. Gastric emptying and orocecal transit time in pregnancy. J Gastroenterol. 2001;36:538–43.
38. Wong CA, McCarthy RJ, Fitzgerald PC, et al. Gastric emptying of water in obese pregnant women at term. Anesth Analg. 2007;105:751–5.
39. Panicker VV, Riyaz N, Balachandran PK. A clinical study of cutaneous changes in pregnancy. J Epidemiol Glob Health. 2017;7:63–70.
40. Thornton P, Douglas J. Coagulation in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2010;24:339–52.
41. Wildsmith JA. Serum pseudocholinesterase, pregnancy and suxamethonium. Anaesthesia. 1972;27:90–1.
42. Evans RT, Wroe JM. Plasma cholinesterase changes during pregnancy. Their interpretation as a cause of suxamethonium-induced apnoea. Anaesthesia. 1980;35:651–4.
43. Datta S, Lambert DH, Gregus J, et al. Differential sensitivities of mammalian nerve fibers during pregnancy. Anesth Analg. 1983;62:1070–2.
44. Choi J, Germond L, Santos AC. Obstetric regional anesthesia. In: Hadzic A, editor. Hadzic's textbook of regional anesthesia and acute pain management. 2nd ed. Beijing: McGraw-Hill Education; 2017.
45. Bosnjak ZJ, Logan S, Liu Y, et al. Recent insights into molecular mechanisms of propofol-induced developmental neurotoxicity: implications for the protective strategies. Anesth Analg. 2016;123:1286–96.
46. Wu J, Bie B, Naguib M. Epigenetic manipulation of brain-derived neurotrophic factor improves memory deficiency induced by neonatal anesthesia in rats. Anesthesiology. 2016;124:624–40.
47. U.S. Food and Drug Administration. FDA drug safety communication: FDA review results in new warnings about using general anesthetics and sedation drugs in young children and pregnant women; 2016. https://www.fda.gov/media/101937/download. Accessed 29 Oct 2020.
48. Sun LS, Li G, Miller TL, et al. Association between a single general anesthesia exposure before age 36 months and neurocognitive outcomes in later childhood. JAMA. 2016;315:2312–20.
49. Sun LS. Introduction to "anesthesia and neurodevelopment in children": a supplement from the sixth pediatric anesthesia neurodevelopmental assessment (PANDA) symposium. J Neurosurg Anesthesiol. 2019;31:101–2.
50. Aytuluk HG. Evaluation of advanced behavior guidance techniques used in dentistry: sedation and general anesthesia. Osmangazi J Med. 2020;42:466–73.
51. Heller AR, Heger J, Gama de Abreu M, et al. Cafedrine/theodrenaline in anaesthesia: influencing factors in restoring arterial blood pressure. Anaesthesist. 2015;64:190–6.
52. Chappell D, Helf A, Gayer J, et al. Antihypotensive drugs in cesarean sections: treatment of arterial hypotension with ephedrine, phenylephrine and Akrinor (cafedrine/theodrenaline) during cesarean sections with spinal anesthesia. Anaesthesist. 2019;68:228–38.
53. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, et al.; ESC Scientific Document Group (2018) 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 39:3165–3241.
54. Maltepe F, Arkan A. Effects on the fetus of anesthesia and non-obstetric surgery for obstetric patient. Turkiye Klinikleri J Surg Med Sci. 2006;2:23–31.

55. Brown WU, Bell GC, Alper MH. Acidosis, local anesthetics and the newborn. Obstet Gynecol. 1976;48:27–30.
56. Okeagu CN, Anandi P, Gennuso S, et al. Clinical management of the pregnant patient undergoing non-obstetric surgery: review of guidelines. Best Pract Res Clin Anaesthesiol. 2020;34:269–81.
57. Kuczkowski KM. Nonobstetric surgery during pregnancy: what are the risks of anesthesia? Obsest Gynecol Surv. 2004;59:52–6.
58. van de Velde M, de Buck F. Anesthesia for non-obstetric surgery in the pregnant patient. Minerva Anestesiol. 2007;73:235–40.
59. Visser BC, Glasgow RE, Mulvihill KK, et al. Safety and timing of nonobstetric abdominal surgery in pregnancy. Dig Surg. 2001;18:409–17.
60. Fisher SC, Siag K, Howley MM, et al. Maternal surgery and anesthesia during pregnancy and risk of birth defects in the National Birth Defects Prevention Study, 1997-2011. Birth Defects Res. 2020;112:162–74.
61. Cohen-Kerem R, Railton C, Oren D, et al. Pregnancy outcome following non-obstetric surgical intervention. Am J Surg. 2005;190:467–73.
62. Brodsky JB, Cohen EN, Brown BW Jr, et al. Surgery during pregnancy and fetal outcome. Am J Obstet Gynecol. 1980;138:1165–7.
63. Duncan PG, Pope WD, Cohen MM, et al. Fetal risk of anesthesia and surgery during pregnancy. Anesthesiology. 1986;64:790–4.
64. Ravindra GL, Madamangalam AS, Seetharamaiah S. Anaesthesia for non-obstetric surgery in obstetric patients. Indian J Anaesth. 2018;62:710–6.
65. U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research. Pregnancy, lactation, and reproductive potential: labeling for human prescription drug and biological products—content and format guidance for industry; 2020. https://www.fda.gov/media/90160/download. Accessed 29 Oct 2020.
66. Department of Health and Human Services Food and Drug Administration. In: Clinical pharmacology section of labeling for human prescription drug and biological products. Guidance for industry. Federal Register. 2016;81(233):87563–87565. Available online via the Government Publishing Office (www.gpo.gov). https://www.govinfo.gov/content/pkg/FR-2014-12-04/pdf/2014-28241.pdf. Accessed 29 Oct 2020.
67. Po' G, Olivieri C, Rose CH, et al. Intraoperative fetal heart monitoring for non-obstetric surgery: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2019;238:12–9.
68. Kilpatrick CC, Puig C, Chohan L, et al. Intraoperative fetal heart rate monitoring during nonobstetric surgery in pregnancy: a practice survey. South Med J. 2010;103:212–5.
69. Yamashita M, Hayashi S, Endo M, et al. Incidence and risk factors for recurrent spontaneous preterm birth: a retrospective cohort study in Japan. J Obstet Gynaecol Res. 2015;41:1708–14.
70. Wikner BN, Stiller CO, Bergman U, et al. Use of benzodiazepines and benzodiazepine receptor agonists during pregnancy: neonatal outcome and congenital malformations. Pharmacoepidemiol Drug Saf. 2007;16:1203–10.
71. Dolovich LR, Addis A, Vaillancourt JM, et al. Benzodiazepine use in pregnancy and major malformations or oral cleft: meta-analysis of cohort and case-control studies. BMJ. 1998;317:839–43.
72. Kuczkowski KM. The safety of anaesthetics in pregnant women. Expert Opin Drug Saf. 2006;5:251–64.
73. White LD, Hodsdon A, An GH, et al. Induction opioids for caesarean section under general anaesthesia: a systematic review and meta-analysis of randomised controlled trials. Int J Obstet Anesth. 2019;40:4–13.
74. Guignard B, Bossard AE, Coste C, et al. Acute opioid tolerance: intraoperative remifentanil increases postoperative pain and morphine requirement. Anesthesiology. 2000;93:409–17.
75. Devroe S, van de Velde M, Rex S. General anesthesia for caesarean section. Curr Opin Anaesthesiol. 2015;28:240–6.

76. Patrick SW, Barfield WD, Poindexter BB, Committee on Fetus and Newborn, Committee on Substance Use and Prevention. Neonatal opioid withdrawal syndrome. Pediatrics. 2020;146(5):e2020029074. https://doi.org/10.1542/peds.2020-029074.
77. Lind JN, Interrante JD, Ailes EC, et al. Maternal use of opioids during pregnancy and congenital malformations: a systematic review. Pediatrics. 2017;139:e20164131. https://doi.org/10.1542/peds.2016-4131.
78. Peck T, Williams M (2008) Core drugs in anaesthetic practice. In: Peck T, Hill S (Authors) Pharmacology for anaesthesia and intensive care, 3rd edn. Cambridge: Cambridge University Press.
79. Gin T. Pharmacology during pregnancy and lactation. In: Chestnut DH, editor. Chestnut's obstetric anesthesia: principles and practice. 6th ed. Philadelphia: Elsevier; 2019.
80. Sachs HC, Committee on Drugs. The transfer of drugs and therapeutics into human breast milk: an update on selected topics. Pediatrics. 2013;132:796–809.
81. Mitchell J, Jones W, Winkley E, et al. Guideline on anaesthesia and sedation in breastfeeding women 2020: guideline from the Association of Anaesthetists. Anaesthesia. 2020;75:1482–93.
82. Kan RE, Hughes SC, Rosen MA, et al. Intravenous remifentanil: placental transfer maternal and neonatal effects. Anesthesiology. 1998;88:1467–74.
83. Ito S. Opioids in breast milk: pharmacokinetic principles and clinical implications. J Clin Pharmacol. 2018;58:151–63.
84. Minami K, Uezono Y, Ueta Y. Pharmacological aspects of the effects of tramadol on G-protein coupled receptors. J Pharmacol Sci. 2007;103:253–60.
85. U.S. Food and Drug Administration. Codeine and tramadol medicines: drug safety communication—restricting use in children, recommending against use in breastfeeding women; 2017. https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm554029.htm. Accessed 29 Oct 2020.
86. Wenzel V, Lindner KH. Best pharmacological practice in prehospital intubation. Lancet. 2009;374:267–826.
87. Downing JW, Buley RJ, Brock-Utne JG, et al. Etomidate for induction of anaesthesia at caesarean section: comparison with thiopentone. Br J Anaesth. 1979;51:135–40.
88. Rosen MA. Nitrous oxide for relief of labor procedure systemic review. Am J Obstet Gynecol. 2002;186:110–25.
89. Leighton BL, Cheek TG, Gross JB, et al. Succinylcholine pharmacodynamics in peripartum patients. Anesthesiology. 1986;64:202–5.
90. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients. Anesthesiology. 1993;79:913–8.
91. Clark RB, Brown MA, Lattin DL. Neostigmine, atropine, and glycopyrrolate: does neostigmine cross the placenta? Anesthesiology. 1996;84:450–2.
92. Amorim P, Lagarto F, Gomes B, et al. Neostigmine vs. sugammadex: observational cohort study comparing the quality of recovery using the postoperative quality recovery scale. Acta Anaesthesiol Scand. 2014;58:1101–10.
93. Yellon SM, Dobyns AE, Beck HL, et al. Loss of progesterone receptor-mediated actions induce preterm cellular and structural remodeling of the cervix and premature birth. PLoS One. 2013;8:e81340. https://doi.org/10.1371/journal.pone.0081340.
94. Et T, Topal A, Erol A, Tavlan A, et al. The effects of sugammadex on progesterone levels in pregnant rats. Balkan Med J. 2015;32:203–7.
95. Richardson MG, Raymond BL. Sugammadex administration in pregnant women and in women of reproductive potential: a narrative review. Anesth Analg. 2020;130:1628–37.
96. Howie WO, McMullen PC. Breastfeeding problems following anesthetic administration. J Perinat Educ. 2006;15:50–7.
97. Hale TW. Anesthetic medications in breastfeeding mothers. J Hum Lact. 1999;15:185–94.
98. Liew Z, Ritz B, Rebordosa C, et al. Acetaminophen use during pregnancy, behavioral problems, and hyperkinetic disorders. JAMA Pediatr. 2014;168:313–20.

99. Magnus MC, Karlstad O, Haberg SE, et al. Prenatal and infant paracetamol exposure and development of asthma: the Norwegian Mother and Child Cohort Study. Int J Epidemiol. 2016;45:512–22.
100. Migliore E, Zugna D, Galassi C, et al. Prenatal paracetamol exposure and wheezing in childhood: causation or confounding? PLoS One. 2015;10:e0135775. https://doi.org/10.1371/journal.pone.0135775.
101. Hauspurg A, Sutton E, Catov J, et al. Applying the new ACC/AHA aspirin effect on adverse pregnancy outcomes associated with stage 1 hypertension in a high-risk cohort. Hypertension. 2018;72:202–7.
102. Lamont T, Coates T, Mathew D, et al. Checking for pregnancy before surgery: summary of a safety report from the National Patient Safety Agency. BMJ. 2010;341:3402. https://doi.org/10.1136/bmj.c3402.
103. Apfelbaum JL, Connis RT, Nickinovich DG, et al. Practice advisory for preanesthesia evaluation. An updated report by the American Society of Anesthesiologists task force on preanesthesia evaluation. Anesthesiology. 2012;116:522–38.
104. American Society of Anesthesiologists. Pregnancy testing prior to anesthesia and surgery; 2016. https://www.asahq.org/standards-and-guidelines/pregnancy-testing-prior-to-anesthesia-and-surgery. Accessed 29 Oct 2020.
105. O'Sullivan G. Gastric emptying during pregnancy and the puerperium. Int J Obstet Anesth. 1993;2:216–24.
106. Nedjlova M, Johnson T. Anaesthesia for non-obstetric procedures during pregnancy. Continuing Educ Anaesthesia Crit Care Pain. 2012;12:203–6.
107. van de Putte P, Perlas A. Ultrasound assessment of gastric content and volume. Br J Anaesth. 2014;113:12–22.
108. Balki M, Cooke ME, Dunington S, et al. Unanticipated difficult airway in obstetric patients: development of a new algorithm for formative assessment in high-fidelity simulation. Anesthesiology. 2012;117:883–97.
109. Mushambi MC, Kinsella SM, Popat M, et al. Obstetric Anaesthetists' association and difficult airway society guidelines for the management of difficult and failed tracheal intubation in obstetrics. Anaesthesia. 2015;70:1286–306.
110. Bordoni L, Parsons K, Rucklidge MWM. Obstetric airway management. Update in Anaesthesia. 2019;34:7–13.
111. Ovassapian A, Salem MR. Sellick's maneuver: to do or not do. Anesth Analg. 2009;109:1360–2.
112. Zheng BX, Zheng H, Lin XM. Ultrasound for predicting difficult airway in obstetric anesthesia: protocol and methods for a prospective observational clinical study. Medicine (Baltimore). 2019;98:17846. https://doi.org/10.1097/MD.0000000000017846.
113. Kristensen MS, Teoh WH, Rudolph SS. Ultrasonographic identification of the cricothyroid membrane: best evidence, techniques, and clinical impact. Br J Anaesth. 2016;117:39–46.
114. Paranjothy S, Griffiths JD, Broughton HK, et al. Interventions at caesarean section for reducing the risk of aspiration pneumonitis. Cochrane Database Syst Rev. 2014;2:CD004943. https://doi.org/10.1002/14651858.CD004943.pub4.
115. Bernhard M, Becker TK, Gries A, et al. The first shot is often the best shot: first-pass intubation success in emergency airway management. Anesth Analg. 2015;121:1389–93.
116. Scott-Brown S, Russell R. Video laryngoscopes and the obstetric airway. Int J Obstet Anesth. 2015;24:137–46.
117. Martin E, Vickers B, Landau R, et al. ABM clinical protocol #28, peripartum analgesia and anesthesia for the breastfeeding mother. Breastfeed Med. 2018;13:164–71.
118. Tobolic TJ. Primum non nocere breastfeeding. Breastfeed Med. 2019;14:77–8.
119. Zelop CM, Grimes EP. Cardiopulmonary resuscitation in pregnancy. In: Field JM, Kudenchuk PJ, O'Connor RE, editors. The textbook of emergency cardiovascular care and CPR. Philadelphia: Wolters Kluwer; 2009.
120. Zelop CM, Einav S, Mhyre JM, et al.; American Heart Association's Get With the Guidelines-Resuscitation Investigators. Characteristics and outcomes of maternal cardiac arrest: a descriptive analysis of get with the guidelines data. Resuscitation. 2018;132:17–20.

121. Vanden Hoek TL, Morrison LJ, Shuster M, et al. Part 12: cardiac arrest in special situations: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2011;122:829–61.
122. Kikuchi J, Deering S. Cardiac arrest in pregnancy. Semin Perinatol. 2018;42:33–8.
123. Jeejeebhoy FM, Zelop CM, Lipman S, et al.; American Heart Association Emergency Cardiovascular Care Committee, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Diseases in the Young, and Council on Clinical Cardiology. Cardiac arrest in pregnancy: a scientific statement from the American Heart Association. Circulation. 2015;132:1747–1773.
124. Yun JG, Lee BK. Spatial relationship of the left ventricle in the supine position and the left lateral tilt position (implication for cardiopulmonary resuscitation in pregnant patients). Fire Sci Eng. 2013;27:75–9.
125. Archer TL, Suresh P, Shapiro AE. Cardiac output measurement, by means of electrical velocimetry, may be able to determine optimum maternal position during gestation, labour and caesarean delivery, by preventing vena caval compression and maximising cardiac output and placental perfusion pressure. Anaesth Intensive Care. 2011;39:308–11.
126. Apfelbaum JL, Hagberg CA, Caplan RA, et al., American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists task force on management of the difficult airway. Anesthesiology. 2013;118:251–270.
127. Mhyre JM, Healy D. The unanticipated difficult intubation in obstetrics. Anesth Analg. 2011;112:648–52.
128. Panchal AR, Berg KM, Hirsch KG, et al. 2019 American Heart Association focused update on advanced cardiovascular life support: use of advanced airways, vasopressors, and extracorporeal cardiopulmonary resuscitation during cardiac arrest: an update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2019;140:881–94.
129. Soar J, Maconochie I, Wyckoff MH, et al. 2019 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations: summary from the basic life support; advanced life support; pediatric life support; neonatal life support; education, implementation, and teams; and first aid task forces. Circulation. 2019;140:826–80.
130. Soar J, Nicholson TC, Parr MJ, et al.; International Liaison Committee on Resuscitation (ILCOR) Advanced Life Support Task Force. Advanced airway management during adult cardiac arrest: consensus on science with treatment recommendations; 2019. https://costr.ilcor.org/document/advanced-airway-management-during-adult-cardiac-arrest. Accessed 29 Oct 2020.
131. Boet S, Duttchen K, Chan J, et al. Cricoid pressure provides incomplete esophageal occlusion associated with lateral deviation: a magnetic resonance imaging study. J Emerg Med. 2012;42:606–11.
132. Neumar RW, Otto CW, Link MS, et al. Part 8: adult advanced cardiovascular life support: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2010;122:729–67.
133. Svinos H. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary, BET 1: emergency caesarean section in cardiac arrest before the third trimester. Emerg Med J. 2008;25:764–5.
134. Finegold H, Darwich A, Romeo R, et al. Successful resuscitation after maternal cardiac arrest by immediate cesarean section in the labor room. Anesthesiology. 2002;96:1278.
135. Cardosi RJ, Porter KB. Cesarean delivery of twins during maternal cardiopulmonary arrest. Obstet Gynecol. 1998;92:695–7.
136. Cobb B, Lipman S. Cardiac arrest: obstetric CPR/ACLS. Clin Obstet Gynecol. 2017;60:425–30.