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Perioperative management of pregnant women undergoing nonobstetric surgery

ABSTRACT

Nonobstetric surgery during pregnancy should be avoided if possible, but when surgery is required, an obstetrician should be part of the perioperative team. In general, preoperative assessment is similar regardless of whether a woman is pregnant, but cardiovascular, pulmonary, hematologic, and renal changes of pregnancy can increase surgical risk and must be taken into account. Special management considerations include pregnancy-associated laboratory changes, timing of surgery, anesthesia choice, intubation precautions, patient positioning, preoperative blood typing, intraoperative fetal monitoring, and venous thromboembolism prophylaxis.

KEY POINTS

Surgery increases the risk of complications in pregnancy, including preterm delivery.

Surgery that cannot wait until after delivery should be conducted during the second trimester, if possible.

During surgery, pregnant women should be placed in the left lateral tilt position at 30° to avoid vena cava compression.

Neuroaxial anesthesia is preferred if possible.

Low-molecular-weight heparin in prophylactic doses is recommended perioperatively to prevent venous thromboembolism.

IMPORTANT PHYSIOLOGIC CHANGES take place during pregnancy that optimize maternal and fetal outcomes but increase risk during surgery. Accommodating normal changes and identifying and managing risk factors should guide perioperative planning.

This article reviews physiologic changes in pregnancy, implications for perioperative management of nonobstetric surgery, and practical notes for clinical management.

■ NONOBSTETRIC SURGERY IN PREGNANCY IS RARE AND RISKY

From 0.2% to 2.0% of pregnant women undergo nonobstetric surgery.^{1,2} In order of frequency, the most common procedures are appendectomy, cholecystectomy, adnexal surgery (for torsion or masses), trauma repair, small-bowel obstruction surgery, and breast surgery.²⁻⁴

The American College of Surgeons National Surgical Quality Improvement Program reported a postoperative complication rate of 5.8% in pregnancy. Complications included reoperation within 30 days (3.6%), infections (2%), wound problems (1.4%), respiratory complications (2%), thromboembolic complications (0.5%), transfusion requirements (0.2%), and death (0.25%).⁴

A study of 5,591 pregnant women in Taiwan⁵ found that the rates of the following postoperative complications were higher than among nonpregnant women:

- Sepsis (odds ratio [OR] 1.75, 95% confidence interval [CI] 1.47–2.07)
- Pneumonia (OR 1.47, 95% CI 1.01–2.13)

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TABLE 1

Benign cardiovascular findings in pregnancy

Physical examination

- Increased intensity of arterial pulses
- Cephalic and lateral displacement of the point of maximum impulse
- Prominent splitting of the second heart sound
- Systolic murmur in the pulmonary and tricuspid areas
- Enhancement of preexisting murmurs
- Systolic-diastolic murmur heard over 1 or both breasts ("mammary souffle")¹⁰

Electrocardiogram

- Left axis deviation
- Left atrial dilatation
- Q-wave and T-wave inversion in III
- Q wave in aVF
- T-wave inversion in V₁, V₂, and V₃

- Urinary tract infection (OR 1.29, 95% CI 1.08–1.54)
- Death (OR 3.94, 95% CI 2.62–5.92).

One of the most common and feared complications from the obstetric perspective is preterm delivery. In a series of 86 pregnant women who underwent nonobstetric surgery in 1992 through 2014, the rate was 41% despite low rates of intraoperative and immediate postoperative complications.⁶

CARDIOVASCULAR CONSIDERATIONS

Pregnancy affects the cardiovascular system in several ways that are important to understand. The leading cause of pregnancy-related death in the United States is cardiovascular disease, with 17.2 deaths per 100,000 live births in 2015.⁷ Pregnancy can unmask underlying congenital cardiac disease or an undiagnosed cardiomyopathy.⁸

Increased blood flow, vasodilation

In pregnancy, cardiac output increases by 40% due to an increase in plasma volume (which

also leads to dilutional anemia), the basal heart rate increases by 10%, and vasodilation leads to a 10- to 20-mm Hg reduction in systemic blood pressure.⁹ These changes lead to an increased hypotensive response to both general and spinal anesthesia.²

Cardiovascular examination reveals multiple signs of increased blood flow (Table 1).¹⁰

Note. A persistent third heart sound (gallop) or any diastolic murmur is abnormal and warrants immediate assessment.²

Special cardiovascular assessment not usually needed

American Heart Association and American College of Cardiology 2014 guidelines for preoperative cardiac evaluation for noncardiac surgery advise the same approach for pregnant and nonpregnant patients.¹¹ Obstetric patients rarely need cardiovascular diagnostic studies.

Several electrocardiographic changes (Table 1) can be attributed to heart elevation by the enlarged uterus and to increased blood volume.¹²

Echocardiography can be safely used in pregnancy.¹³ Its indications are to assess underlying congenital heart disease, heart valve disorders, a new nonphysiologic murmur, or a third or fourth heart sound.¹⁴

Note. For pregnant women with heart disease, the CARPREG (Cardiac Disease in Pregnancy) II index is useful for preoperative evaluation (Table 2).⁸

RESPIRATORY CONSIDERATIONS

The growing uterus pushes up on the diaphragm, restricting the lungs and reducing functional residual capacity by about 20% when the patient is upright and 50% to 70% when recumbent.^{15,16} Minute volume and tidal volume increase during pregnancy by about 35%, predisposing patients to respiratory alkalosis.¹⁷ Thus, one would expect faster induction with inhalation anesthesia.²

Despite the expected pulmonary changes associated with pregnancy, tachypnea should be regarded as unusual and warrants formal assessment. If the patient suddenly begins breathing rapidly, evaluate for pulmonary embolism.¹⁷

Preterm delivery is a common and feared complication of surgery

TABLE 2

Cardiac Disease in Pregnancy (CARPREG) II risk index

Predictor	Points
History of cardiac events or arrhythmia	3
Baseline New York Heart Association class III/IV or cyanosis	3
Mechanical heart valve	3
Decreased ventricular function	2
History of mitral or aortic valve dysfunction	2
Pulmonary hypertension	2
Coronary artery disease	2
Aortic disease	2
Late pregnancy assessment	1
No previous intervention for existing cardiac problem	1

Score	Incidence of adverse cardiac events
0 or 1	5%
2	10%
3	15%
4	22%
> 4	41%

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Pulmonary preoperative assessment and optimization

Attempts to place an endotracheal tube fail in about 1 in 300 cases in pregnancy, a rate about 10 times higher than in the general population.^{18,19}

Anesthesiologists should consider reduced functional residual capacity, possible increased airway edema, and reduced oxygen delivery secondary to the physiologic anemia of pregnancy as risk factors for hypoxemic respiratory failure.²

No formal guidelines have been published for preoperative pulmonary assessment in pregnancy. The most important purpose of assessment is to identify risks of a difficult airway and aspiration. The American Society of Anesthesiologists updated its general practice guidelines for managing difficult airways in 2003,²⁰ and Mhyre et al²¹ proposed an algorithm in 2011 specifically for difficult intubations in obstetrics.

The 4-class Mallampati classification is used to assess the airway. Class 3 (ie, with the patient sticking out her tongue, the soft and hard palate and base of the uvula are visible but not the tonsils, or only the hard palate is visible) indicates increased likelihood that mask ventilation and endotracheal intubation will be difficult. For patients in this class, all airway protective measures should be taken.^{21,22}

For patients who must be supine and in anticipation of periods of apnea (eg, before endotracheal intubation), supplemental oxygen should be used, and lung expansion maneuvers are strongly recommended to prevent atelectasis.^{17,23}

In anticipation of a “difficult” airway, consider smaller endotracheal tubes and fiberoptic intubation.²

RENAL CONSIDERATIONS

Anatomic changes of a pregnant uterus cause some degree of urinary stasis and dilation of

Pregnancy can unmask underlying congenital cardiac disease or undiagnosed cardiomyopathy

TABLE 3

Changes in laboratory values in pregnancy

Laboratory test	Change in pregnancy	Implication
Serum creatinine and blood urea nitrogen	Decrease due to increased glomerular filtration	Nonpregnancy normal values may indicate developing renal failure
Urine protein	Hyperfiltration leads to proteinuria	Small increases are normal, but > 300 mg/24 hours may indicate preeclampsia
Alkaline phosphatase	Increases due to placental production	
Bilirubin and aminotransferases	Decrease	Nonpregnancy normal values of aminotransferases may indicate HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome
Thyroid-stimulating hormone	Decreases early, gradually normalizes	Free triiodothyronine and free thyroxine levels are stable and are better indicators of thyroid function than total values
Corticotropin and cortisol	Increase	Serum or salivary cortisol is not a reliable indicator of pathology

If the onset of tachypnea is sudden, evaluate for pulmonary embolism

the pyelocaliceal system, increasing the propensity to develop urinary tract infections.^{2,24}

In addition, a 50% higher glomerular filtration rate and other pregnancy-associated changes may cause specific laboratory values to either increase or decrease, so it is important to be aware of the “pregnancy normal” (Table 3).^{24–26} Increased plasma volume dilutes serum levels of albumin by an average of 1 mg/dL. This may cause serum calcium levels to decrease, although ionized calcium stays in the normal range.²⁶

HEMATOLOGIC CONSIDERATIONS

In pregnancy, the red blood cell mass volume increases, but the plasma volume increases more, leading to dilutional anemia.²⁷ At the same time, pregnancy is associated with a 6- to 10-fold higher risk of deep vein thrombosis than in age-matched women.²⁸ This procoagulant state is attributed to increased production of clotting factors I, II, V, VII, VIII, X, and XII and a reduction of factors of the fibrinolytic system.²⁹

Therefore, perioperative management should include prophylaxis against deep vein thrombosis³⁰ with low-molecular-weight heparin (LMWH) in prophylactic doses.^{31,32}

Some obstetricians routinely switch anti-

coagulation from LMWH to unfractionated heparin after gestational week 37 in anticipation of labor or emergency cesarean delivery. However, the safety profile of LMWH is superior to that of unfractionated heparin in pregnancy, with lower risks of bleeding, heparin-induced thrombocytopenia, and heparin-associated osteoporosis.³³ In addition, several factors enhance the bioavailability of LMWH: it does not cross the placenta, it is less deactivated by tissue proteins owing to its smaller molecular size,^{34,35} and its half-life and volume of distribution increase in pregnancy.³⁶

Consider Rh blood type

If surgery entails risk of uterine trauma and maternal-fetal hemorrhage, the mother’s blood group should be identified preoperatively.

If the mother is Rh-negative and the fetus is Rh-positive, the mother should be given anti-D immune globulin to minimize or prevent maternal-fetal isoimmunization.³⁷ In general, the American College of Obstetricians and Gynecologists³⁸ recommends giving prophylactic anti-D immune globulin to unsensitized Rh D-negative women at 28 weeks of gestation. After birth, in the case of Rh D-positive neonates, all confirmed unsensitized Rh D-negative women should receive anti-D

immune globulin within 72 hours of delivery (evidence level A).³⁸

Anemia

The Network for the Advancement of Patient Blood Management, Haemostasis, and Thrombosis consensus for management of anemia in pregnancy recommends administration of intravenous iron in patients with severe iron deficiency anemia (hemoglobin < 8 g/dL) or newly diagnosed iron deficiency anemia beyond 34 weeks of gestational age.³⁹ If the patient requires red blood cell transfusion, this should ideally not be influenced by arbitrary hemoglobin levels. In nonbleeding patients, red blood cell transfusion of a single unit can be considered when hemoglobin levels are less than 6 g/dL.

■ GASTROINTESTINAL CONSIDERATIONS

Gastroesophageal reflux is common in pregnant women owing to the growing uterus occupying more abdominal space, as well as progesterone contributing to slowing of gastric emptying time and reduced inferior esophageal sphincter tone.

Perioperative use of prokinetics, antacid medications, and reflux prevention strategies (eg, elevating the head of the bed at least 15°, fasting 8 hours) are recommended.⁴⁰ However, one should avoid enteral particulate antacids (ie, colloid suspensions containing aluminum or magnesium hydroxide), which increase the risk of pneumonitis if aspirated.⁴¹

Pregnant women should be considered to have full gastric content before surgery. If intubation is needed, a rapid sequence intubation protocol is indicated.²

Pregnancy causes several changes in liver function (Table 3).⁴⁰

■ ENDOCRINE CONSIDERATIONS

Hormonal changes during pregnancy are critical to maternal and fetal homeostasis.⁴⁰ Changes occur in multiple systems, including the thyroid, and in glucose and adrenal metabolism.⁴²

Human chorionic gonadotropin is structurally similar to thyroid-stimulating hormone (TSH), resulting in TSH suppression during the first trimester. Human chorionic gonadotropin peaks at the end of the first trimester,

and TSH tends to normalize by the end of pregnancy. Free triiodothyronine and free thyroxine levels tend to remain stable throughout pregnancy, and their measurement is preferred to total hormone levels, given the dilutional decrease of circulating albumin and increase in thyroid-binding globulin.^{42,43}

Pancreatic islet cells tend to hypertrophy, resulting in higher serum insulin levels that contribute to hypoglycemic episodes in early pregnancy. However, placental growth and increased secretion of placental lactogen increase insulin resistance, which may contribute to gestational diabetes in genetically predisposed patients.⁴⁰

The pituitary tends to enlarge by about one-third during pregnancy, although this almost never leads to symptoms of optic chiasm compression. Prolactin levels increase progressively throughout pregnancy, enabling milk production.⁴²

The placenta also produces corticotropin-releasing hormone, which increases the production of corticotropin and cortisol. It may be difficult to distinguish whether increased serum or salivary cortisol indicates a normal or pathologic state.⁴⁴

■ GENERAL PERIOPERATIVE CONSIDERATIONS

Timing of surgery

Elective surgery should be postponed until after delivery, but urgent procedures necessary to save a patient's life should be pursued regardless of pregnancy stage.⁴⁵

Although patients can be reassured that anesthetic gases do not appear to be teratogenic, surgery during the first trimester may affect the rest of the pregnancy.²³ The third trimester poses the highest risk for both mother and fetus; at that time, surgery becomes more technically difficult, and the fetus's higher perfusion needs increase the risk of fetal hypoxia.

If there is a choice, the second trimester is the best time to undergo necessary surgery.

Include an obstetrician on the team

The American College of Obstetricians and Gynecologists and the American Society of Anesthesiologists recommend involving an obstetric specialist to help assess and manage pregnant women requiring any surgical or in-

Risk of failed endotracheal intubation is about 10 times higher in pregnancy

vasive procedure. An obstetric care provider with cesarean delivery privileges and a pediatric or neonatologist team should be available during the procedure.

Minimally invasive is best

Particularly for patients needing abdominal surgery, a laparoscopic approach is preferred to reduce risk of fetal complications.^{46,47}

Avoid supine positioning

During the second and third trimesters of pregnancy, the uterus compresses the inferior vena cava when the patient lies flat, reducing venous return by about 30%, with a consequent decrease in cardiac output and placental perfusion. For these reasons, patients should lie on their side during surgery.⁴⁸ In a study using magnetic resonance imaging,⁴⁹ the maximum aortocaval decompression was achieved with a left-lateral tilt position of 30°.

The anesthesiologist should place the patient in a 30° left lateral decubitus position and maintain normovolemia, oxygen saturation greater than 95%, and normal arterial pressure of carbon dioxide.^{45,50}

Preoperative diagnostic tests

The most commonly required tests include hematocrit and preoperative blood type and antibody screen. Otherwise, routine preoperative testing is not justified for most patients with no active systemic comorbidity.^{23,51} The need for other studies is based on risk factors and predisposing conditions.^{2,12,52}

Fetal monitoring

Viable fetuses older than 23 weeks gestational age (or > 22 weeks in some centers) should have continuous monitoring and simultaneous contraction activity monitoring throughout any surgical procedure.

ANESTHESIA CONSIDERATIONS

Identifying risk factors for complications associated with induction of anesthesia is paramount. In addition to a physical assessment, clinicians should ask about personal and family history of bleeding disorders, coagulopathy, and complications related to anesthesia (eg, malignant hyperthermia).²³

Risk of anesthetic morbidity and mortality in pregnancy are most associated with airway

edema, restrictive lung physiology, and aspiration.⁵³ Other risk factors are eclampsia or preeclampsia, postpartum shock, pulmonary embolism, obesity, uncontrolled arterial hypertension, and emergency surgery.^{54,55}

Increasing use of regional anesthesia instead of general anesthesia⁵⁶ during delivery has led to reduced mortality. Hawkins et al⁵⁷ found a 59% reduction (from 2.9 to 1.2 deaths per million patients) in anesthesia-related maternal mortality in the years 1991 to 2002 compared with 1979 to 1990. The relative risk of death during general anesthesia decreased from 6.7 before 1996 to 1.7 after that year. The improvements were associated with reduction in general anesthesia, as regional anesthesia rates increased during that time.

Neuraxial anesthesia preferred

Neuraxial anesthesia is preferred if possible. However, specific changes in the central nervous system affect neuraxial anesthesia during pregnancy. Epidural vein engorgement and reduced epidural-space volume increase the spread of epidurally injected local anesthetics and also the risk of a bloody spinal tap.²

Anticoagulation considerations for neuraxial anesthesia are similar in pregnant and nonpregnant patients. Before performing a neuraxial procedure, it is recommended to wait at least 12 hours (for prophylactic dosages) and 24 hours (for full anticoagulation dosages) after administering the last dose of LMWH, and 6 hours after an unfractionated heparin infusion.³¹

Aspirin use

Surgery may proceed for patients treated with low-dose aspirin. The Collaborative Low-Dose Aspirin Study in Pregnancy⁵⁸ did not find increased bleeding risk in patients taking aspirin with spinal anesthesia, although they did find a nonsignificant increase in the need for allogeneic blood transfusion. A randomized comparison of aspirin against placebo found no association of low-dose aspirin during pregnancy with epidural anesthesia complications.⁵⁹

TAKE-HOME POINTS

The perioperative assessment of the pregnant patient undergoing surgery is similar to that of the nonpregnant patient; however, the physi-

A persistent third heart sound (gallop) or any diastolic murmur is abnormal

ologic changes of pregnancy must be taken into consideration.

Diagnostic and therapeutic decisions should not neglect the mother and not withhold needed care for her with the purpose of protecting the fetus.

It is preferred to wait until the postpartum period for any elective surgery. However, if surgery is necessary, it can best be done during the second trimester. Emergency surgery should be pursued regardless of the gestational age. The preferred approach for abdominal

surgery is by laparoscopy.

The preferred anesthetic approach is neuroaxial anesthesia if possible.

Close communication among the internist, obstetric-gynecology specialist, and anesthesiologist is paramount to optimize the resources and clinical outcomes of the surgical obstetric patient.

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REFERENCES

- Barron WM. The pregnant surgical patient: medical evaluation and management. *Ann Intern Med* 1984; 101(5):683–691. doi:10.7326/0003-4819-101-5-683
- Ravindra GL, Madamangalam AS, Seetharamaiah S. Anaesthesia for non-obstetric surgery in obstetric patients. *Indian J Anaesth* 2018; 62(9):710–716. doi:10.4103/ijana.463_18
- Gilo NB, Amini D, Landy HJ. Appendicitis and cholecystitis in pregnancy. *Clin Obstet Gynecol* 2009; 52(4):586–596. doi:10.1097/GRF.0b013e3181c11d10
- Erekson EA, Brousseau EC, Dick-Biascoechea MA, Ciarleglio MM, Lockwood CJ, Pettker CM. Maternal postoperative complications after nonobstetric antenatal surgery. *J Matern Fetal Neonatal Med* 2012; 25(12):2639–2644. doi:10.3109/14767058.2012.704445
- Huang SY, Lo PH, Liu WM, et al. Outcomes after nonobstetric surgery in pregnant patients: a nationwide study. *Mayo Clin Proc* 2016; 91(9):1166–1172. doi:10.1016/j.mayocp.2016.06.021
- Baldwin EA, Borowski KS, Brost BC, Rose CH. Antepartum non-obstetrical surgery at ≥ 23 weeks' gestation and risk for preterm delivery. *Am J Obstet Gynecol* 2015; 212(2):232.e1–232.e2325. doi:10.1016/j.ajog.2014.09.001
- Mehta LS, Warnes CA, Bradley E, et al. Cardiovascular considerations in caring for pregnant patients: a scientific statement from the American Heart Association. *Circulation* 2020; May 4. doi:10.1161/CIR.0000000000000772
- Silversides CK, Grewal J, Mason J, et al. Pregnancy outcomes in women with heart disease: the CARPREG II Study. *J Am Coll Cardiol* 2018; 71(21):2419–2430. doi:10.1016/j.jacc.2018.02.076
- Ouzounian JG, Elkayam U. Physiologic changes during normal pregnancy and delivery. *Cardiol Clin* 2012; 30(3):317–329. doi:10.1016/j.ccl.2012.05.004
- Napodano RJ. The functional heart murmur: a wastebasket diagnosis. *J Fam Pract* 1977; 4(4):637–639. PMID:853276
- Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014; 130(24):e278–e333. doi:10.1161/CIR.0000000000000106
- Morton A, Teasdale S. Review article: investigations and the pregnant woman in the emergency department—Part 2: point-of-care ultrasound, electrocardiography, respiratory function tests and radiology. *Emerg Med Australas* 2018; 30(6):749–753. doi:10.1111/1742-6723.12956
- Liu S, Elkayam U, Naqvi TZ. Echocardiography in pregnancy: part 1. *Curr Cardiol Rep* 2016; 18(9):92. doi:10.1007/s11886-016-0760-7
- Narayanan M, Elkayam U, Naqvi TZ. Echocardiography in pregnancy: part 2. *Curr Cardiol Rep* 2016; 18(9):90. doi:10.1007/s11886-016-0761-6
- Hegewald MJ, Crapo RO. Respiratory physiology in pregnancy. *Clin Chest Med* 2011; 32(1):1–13. doi:10.1016/j.ccm.2010.11.001
- Hirnle L, Lysenko L, Gerber H, et al. Respiratory function in pregnant women. *Adv Exp Med Biol* 2013; 788:153–160. doi:10.1007/978-94-007-6627-3_23
- Lee SY, Chien DK, Huang CH, Shih SC, Lee WC, Chang WH. Dyspnea in pregnancy. *Taiwan J Obstet Gynecol* 2017; 56(4):432–436. doi:10.1016/j.tjog.2017.04.035
- Maronge L, Bogod D. Complications in obstetric anaesthesia. *Anaesthesia* 2018; 73(suppl 1):61–66. doi:10.1111/anae.14141
- Hinova A, Fernando R. The preoperative assessment of obstetric patients. *Best Pract Res Clin Obstet Gynaecol* 2010; 24(3):261–276. doi:10.1016/j.bpobgyn.2009.12.003
- 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* 2003; 98(5):1269–1277. doi:10.1097/00005542-200305000-00032
- Mhyre JM, Healy D. The unanticipated difficult intubation in obstetrics. *Anesth Analg* 2011; 112(3):648–652. doi:10.1213/ANE.0b013e31820a91a6
- Cheek TG, Baird E. Anesthesia for nonobstetric surgery: maternal and fetal considerations. *Clin Obstet Gynecol* 2009; 52(4):535–545. doi:10.1097/GRF.0b013e3181c11f60
- Auron M, Duran Castillo M. Manejo perioperatorio de la paciente obstétrica. Spanish. In: Beltran Montoya J, Dueñas García OF, eds. *Manual de Técnicas Quirúrgicas en Obstetricia Basada en Evidencias*. Instituto Nacional de Perinatología, México: McGraw Hill; 2015:525–548.
- Cheung KL, Lafayette RA. Renal physiology of pregnancy. *Adv Chronic Kidney Dis* 2013; 20(3):209–214. doi:10.1053/j.ackd.2013.01.012
- Hussein W, Lafayette RA. Renal function in normal and disordered pregnancy. *Curr Opin Nephrol Hypertens* 2014; 23(1):46–53. doi:10.1097/01.mnh.0000436545.94132.52
- Soma-Pillay P, Nelson-Piercy C, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. *Cardiovasc J Afr* 2016; 27(2):89–94. doi:10.5830/CVJA-2016-021
- Sun D, McLeod A, Gandhi S, Malinowski AK, Shehata N. Anemia in pregnancy: a pragmatic approach. *Obstet Gynecol Surv* 2017; 72(12):730–737. doi:10.1097/OGX.0000000000000510
- Fogarty AE. Management of venous thromboembolism in pregnancy. *Curr Treat Options Cardiovasc Med* 2018; 20(8):69.
- Katz D, Beilin Y. Disorders of coagulation in pregnancy. *Br J Anaesth* 2015; 115(suppl 2):ii75–ii88. doi:10.1093/bja/aeu374
- Kolettis D, Craigo S. Thromboprophylaxis in pregnancy. *Obstet Gynecol Clin North Am* 2018; 45(2):389–402. doi:10.1016/j.ogc.2018.01.007
- Leffert L, Butwick A, Carvalho B, et al. The Society for Obstetric Anesthesia and Perinatology consensus statement on the anesthetic management of pregnant and postpartum women receiving thromboprophylaxis or higher dose anticoagulants. *Anesth Analg* 2018; 126(3):928–944. doi:10.1213/ANE.0000000000002530

32. Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schünemann HJ; American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive summary: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;141(suppl 2): 7S–47S. doi:10.1378/chest.141253
33. Bates SM, Middeldorp S, Rodger M, James AH, Greer I. Guidance for the treatment and prevention of obstetric-associated venous thromboembolism. *J Thromb Thrombolysis* 2016; 41(1):92–128. doi:10.1007/s11239-015-1309-0
34. Romualdi E, Dentali F, Rancan E, et al. Anticoagulant therapy for venous thromboembolism during pregnancy: a systematic review and a meta-analysis of the literature. *J Thromb Haemost* 2013; 11(2):270–281. doi:10.1111/jth.12085
35. Emery S. Anticoagulation in pregnancy: Q&A on low molecular weight heparin. *OBG Manag* 2004; 16(4):31–48.
36. Patel JP, Green B, Patel RK, Marsh MS, Davies JG, Arya R. Population pharmacokinetics of enoxaparin during the antenatal period. *Circulation* 2013; 128(13):1462–1469. doi:10.1161/CIRCULATIONAHA.113.003198
37. Sandler SG, Gottschall JL. Postpartum Rh immunoprophylaxis. *Obstet Gynecol* 2012; 120(6):1428–1438. doi:10.1097/aog.0b013e3182742eba
38. Committee on Practice Bulletins-Obstetrics. Practice Bulletin No. 181: Prevention of Rh D alloimmunization. *Obstet Gynecol* 2017; 130(2):e57–e70. doi:10.1097/AOG.0000000000002232
39. Muñoz M, Peña-Rosas JP, Robinson S, et al. Patient blood management in obstetrics: management of anaemia and haematinic deficiencies in pregnancy and in the post-partum period: NATA consensus statement. *Transfusion Med* 2018; 28(1):22–39. doi:10.1111/tme.12443
40. Tan EK, Tan EL. Alterations in physiology and anatomy during pregnancy. *Best Pract Res Clin Obstet Gynaecol* 2013; 27(6):791–802. doi:10.1016/j.bpobgyn.2013.08.001
41. McKenzie H, Pulley DD. The pregnant patient: assessment and perioperative management. *Anesthesiol Clin* 2016; 34(1):213–222. doi:10.1016/j.anclin.2015.10.016
42. Carlin A, Alfirevic Z. Physiological changes of pregnancy and monitoring. *Best Pract Res Clin Obstet Gynaecol* 2008; 22(5):801–823. doi:10.1016/j.bpobgyn.2008.06.005
43. Alemu A, Terefe B, Abebe M, Biadgo B. Thyroid hormone dysfunction during pregnancy: a review. *Int J Reprod Biomed (Yazd)* 2016; 14(11):677–686. PMID:27981252
44. Feldt-Rasmussen U, Mathiesen ER. Endocrine disorders in pregnancy: physiological and hormonal aspects of pregnancy. *Best Pract Res Clin Endocrinol Metab* 2011; 25(6):875–884. doi:10.1016/j.beem.2011.07.004
45. Committee on Obstetric Practice and the American Society of Anesthesiologists. Committee Opinion No. 696: nonobstetric surgery during pregnancy. *Obstet Gynecol* 2017; 129(4):777–778. doi:10.1097/AOG.0000000000002014
46. Pearl J, Price R, Richardson W, Fanelli R; Society of American Gastrointestinal Endoscopic Surgeons. Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy. *Surg Endosc* 2011; 25(11):3479–3492. doi:10.1007/s00464-011-1927-3
47. Wilasrusmee C, Sukrat B, McEvoy M, Attia J, Thakkinstian A. Systematic review and meta-analysis of safety of laparoscopic versus open appendectomy for suspected appendicitis in pregnancy. *Br J Surg* 2012; 99(11):1470–1478. doi:10.1002/bjs.8889
48. Lees MM, Scott DB, Kerr MG, Taylor SH. The circulatory effects of recumbent postural change in late pregnancy. *Clin Sci* 1967; 32(3):453–465.
49. Higuchi H, Takagi S, Zhang K, Furui I, Ozaki M. 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(2):286–293. doi:10.1097/ALN.0000000000000553
50. Moaveni DM, Birnbach DJ, Ranasinghe JS, Yasin SY. Fetal assessment for anesthesiologists: are you evaluating the other patient? *Anesth Analg* 2013; 116(6):1278–1292. doi:10.1213/ANE.0b013e31828d33c5
51. La Fianza A, Coven G, Preda L, et al. Razionalizzazione dell'esecuzione del radiogramma preoperatorio del torace nell'ostetricia e ginecologia. *Radiol Med* 1997; 94(6):618–621. Italian. PMID:9524599
52. Morton A, Teasdale S. Review article: investigations and the pregnant woman in the emergency department—part 1: laboratory investigations. *Emerg Med Australas* 2018; 30(5):600–609. doi:10.1111/1742-6723.12957
53. Kodali BS, Chandrasekhar S, Bulich LN, Topulos GP, Datta S. Airway changes during labor and delivery. *Anesthesiology* 2008; 108(3):357–362. doi:10.1097/ALN.0b013e31816452d3
54. Panchal S, Arria AM, Labhsetwar SA. Maternal mortality during hospital admission for delivery: a retrospective analysis using a state-maintained database. *Anesth Analg* 2001; 93(1):134–141. doi:10.1097/0000539-200107000-00028
55. Endler GC, Mariona FG, Sokol RJ, Stevenson LB. Anesthesia-related maternal mortality in Michigan, 1972 to 1984. *Am J Obstet Gynecol* 1988; 159(1):187–193. doi:10.1016/0002-9378(88)90519-4
56. Eltzschig HK, Lieberman ES, Camann WR. Regional anesthesia and analgesia for labor and delivery. *N Engl J Med* 2003; 348(4):319–332. doi:10.1056/NEJMra021276
57. Hawkins JL, Chang J, Palmer SK, Gibbs CP, Callaghan WM. Anesthesia-related maternal mortality in the United States: 1979–2002. *Obstet Gynecol* 2011; 117(1):69–74. doi:10.1097/AOG.0b013e31820093a9
58. CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9,364 pregnant women. CLASP (Collaborative Low-dose Aspirin Study in Pregnancy) Collaborative Group. *Lancet* 1994; 343(8898):619–629. PMID:7906809
59. Sibai BM, Caritis SN, Thom E, Shaw K, McNellis D. Low-dose aspirin in nulliparous women: safety of continuous epidural block and correlation between bleeding time and maternal-neonatal bleeding complications. National Institute of Child Health and Human Developmental Maternal-Fetal Medicine Network. *Am J Obstet Gynecol* 1995; 172(5):1553–1557. doi:10.1016/0002-9378(95)90495-6

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