REVIEW ARTICLE

Abdominal Surgery in Pregnancy—an Interdisciplinary Challenge

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SUMMARY

Background: Abdominal operations are performed during ca. 2% of all pregnancies. They represent an unusual situation not only for the patient, but also for the involved surgeons and anesthesiologists. Appendectomy, followed by cholecystectomy are the two most common types of operation performed during pregnancy. Special questions arise with regard to the peri- and intraoperative management and the optimal surgical approach.

Methods: This review is based on pertinent articles retrieved by a selective search in the PubMed database.

Results: The question of laparoscopy versus laparotomy during pregnancy has been addressed to date only in case series and a few meta-analyses. Two meta-analyses have shown a significantly higher rate of miscarriage after laparoscopic, compared to open, appendectomy (relative risk [RR] 1.91, 95% confidence interval [CI] 1.31–2.77). The risk of preterm birth is also somewhat higher after laparoscopic appendectomy according to one meta-analysis on this subject (RR 1.44, 95% CI 0.78–1.76), but significantly lower according to another meta-analysis (2.1% vs. 8.1%, $p < 0.0001$). For cholecystectomy, laparoscopy was associated with a lower miscarriage rate than laparotomy (1 in 89 cases, versus 2 in 69 cases), but with a somewhat higher preterm birth rate (6 in 89 cases, versus 2 in 69 cases). Delay or non-performance of surgery in a patient with appendicitis or cholecystitis can lead to additional hospitalizations, a higher miscarriage rate, premature rupture of the membranes, and preterm birth.

Conclusion: Laparoscopy in experienced hands is safe even during pregnancy, with the recognized advantages of minimally invasive surgery, yet it carries a higher miscarriage rate than laparotomy, with a comparable preterm birth rate. Before surgery, patients should be thoroughly informed about the operation they are about to undergo and the advantages and disadvantages of the available surgical approaches.

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About 2% of pregnant women require surgery during pregnancy for a non-obstetric indication (1, 2).

The physiologic and anatomic changes during pregnancy are so significant that an anesthesiologist would place a non-pregnant patient with the same parameters in a higher perioperative risk group. Many of these changes are based on hormonal factors as well as the mechanical effect of the enlarged uterus; they have important consequences for the surgeon and the anesthesiologist (*Table 1*).

If a pregnant patient requires abdominal surgery, the major issues are the optimal perioperative management and the best surgical approach. In the past, laparotomy was the only option. In recent years, more and more laparoscopic procedures are being done during pregnancy (3).

The goal of this review is to identify the indications and limitations of both laparoscopy (*Box 1*) and laparotomy during pregnancy. The discussion takes into consideration the need for an interdisciplinary approach to such patients. Anesthetic and obstetric challenges and risks, as well as their management, are included.

Methods

A literature search was performed in PubMed. The search includes all meta-analyses, case series and guidelines on abdominal surgery during pregnancy published between 1994 and 2014. Obstetric procedures were excluded.

Indications and operative approaches

The most common non-obstetric operation during pregnancy is an appendectomy (44%), followed by a cholecystectomy (22.3%). In the USA, 64.8% of these intraperitoneal procedures are performed via laparoscopy (3). There is no data on this frequency from Germany. There are no randomized controlled trials (RCTs) for any of the indications discussed below addressing either conservative versus operative management or laparoscopy versus laparotomy. Most publications dealing with these issues are case series. Thus, the level of evidence for the various interventions discussed below is low (*Box 2*).

Appendectomy

McGory et al. discussed 454 pregnant patients who underwent laparoscopy—the largest patient collective

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TABLE 1

Physiologic changes during pregnancy (modified after Kuczkowski [e15])

Physiologic parameter	Change („+“ increase or „-“ reduction in %) in comparison to a non-pregnant woman
Minimum alveolar concentration for inhalation anesthesia (MAC)	- 40
Systemic vascular resistance	- 15
Heart rate	+ 15
Stroke volume	+ 30
Plasma volume	+ 45
Cardiac index	+ 40
Functional residual capacity	- 20
HCO ₃	- 15
paCO ₂	- 15
paO ₂	- 15
Respiratory rate	+ 15
Oxygen consumption	+ 20
Tidal volume	+ 40
Respiratory minute volume	+ 50
Hemoglobin	- 20
Clotting factors	+ 50–200
Glomerular filtration rate	+ 50

studied. These 454 patients were compared to 2679 patients with appendicitis who underwent laparotomy. The information was obtained from a population-based data base in California. The rate of miscarriage was higher with laparoscopy (7%) than with laparotomy (3%) (Odds Ratio [OR]: 2.31; 95% confidence interval [95% CI]: 1.51–3.55). In contrast, the percentage of preterm births was <1% with laparoscopy and 8% after laparotomy (4).

The literature contains conflicting information on this issue. In most other series, the method of approach did not influence the risk of a preterm birth. In one case series, patients who underwent laparoscopy had a preterm birth rate (<37 gestational week) of 18.1%; the stage of pregnancy during which the procedure was performed seemed to play no role (5).

About 33% of the patients in whom appendicitis was suspected had a normal appendix on operation; this is higher than usually encountered (5). Balanced against the frequent unremarkable appendices are those cases that smolder and come to operation late with dramatic consequences.

Two recent meta-analyses have confirmed the statistically significantly increased risk of miscarriages with laparoscopic appendectomy as compared to an open procedure. In the study of Wilasrusmee et al. from 2012 on 3415 women (n = 599 laparoscopies versus n = 2816 laparotomies), the relative risk for a

miscarriage following laparoscopy was RR = 1.91 (95% CI: 1.31–2.77). The risk of a preterm birth was also elevated but not to a statistically significant degree (RR = 1.44, 95% CI: 0.78–1.76). This study showed no statistically significant differences in length of hospitalization, wound infection rate, birth weight, length of operation, or Apgar score.

Walsh et al. analyzed 28 studies including 637 patients who underwent laparoscopic appendectomy. Their data also showed a significantly higher miscarriage rate for laparoscopy with 5.6% as compared to laparotomy with 3.1%. In contrast to the first meta-analysis, the preterm birth rate was significantly higher with laparotomy as compared to laparoscopy (8.1% versus 2.1%). The miscarriage rate and preterm birth rate did not significantly vary with the trimester (Miscarriage rate in 1st trimester 3.8%; in 2nd trimester, 2.6%; in 3rd trimester, 0%; p = 0.55; preterm birth rate in 1st trimester 4.3%; in 2nd trimester, 11.3%; in 3rd trimester, 13.6%; p = 0.32) (6, 7).

Because of the increased risk of miscarriage following a laparoscopic appendectomy, an open approach should be favored. Nevertheless, the guidelines of the Society of American Gastrointestinal and Endoscopic Surgeons recommend laparoscopic surgery for a pregnant women with suspected appendicitis (8). There are no other guidelines addressing this issue or the other indications discussed below.

Cholecystectomy

Laparoscopic cholecystectomy is the approach recommended by the above-mentioned US guidelines for pregnant patients with gall bladder disease, regardless of the stage of pregnancy (8). Although in the past a conservative approach was preferred for symptomatic cholelithiasis, today early surgical intervention is favored (8). A conservative approach may lead to recurrent symptoms later in pregnancy; the risk varies with the stage of pregnancy and the disorder, but for example 92% of women with gall stones in the first trimester can expect further troubles (9). Delayed or neglected surgical intervention leads to increased hospitalization rates, a higher miscarriage rate, premature rupture of membranes, and an increased rate of preterm births (10–13). Conservative management of symptomatic gall stones in pregnancy leads to recurrent symptoms in more than 50% of cases. In a study of almost 30 000 pregnancies, 47 women (0.16%) had symptoms including biliary colic (n = 33), acute cholecystitis (n = 12) or pancreatitis (n = 2). In 36% of cases, after a trial of conservative management, an operation was required for biliary colic (n = 10), acute cholecystitis (n = 6) or pancreatitis (n = 1) (14). Pancreatitis during pregnancy leads to a miscarriage in 0–60% of cases (15, 16). The most common causes for acute pancreatitis during pregnancy are gall stones (60–100%), alcohol abuse and hypertriglyceridemia (17).

Because of the increased morbidity associated with untreated gall bladder disease during pregnancy as described below, surgical intervention is recommended.

Women who are first treated conservatively during pregnancy have a significantly higher rate of recurrent symptoms (60% versus 13%), are more likely to be hospitalized (1.5 versus 1.2 hospitalizations), and visit their physician more often (1.7 versus 1.1 visits) (18). Because of the good results and lower morbidity, primary laparoscopic surgery is recommended (8, 19). A review of several case series comparing laparoscopy with laparotomy identified a lower miscarriage rate for laparoscopy (1/89 cases with laparoscopy versus 2/69 after laparotomy) but somewhat more preterm births (6/89 with laparoscopy versus 2/69 after laparotomy) (9). Once again, we emphasize that there are no RCTs comparing laparoscopic versus open cholecystectomy during pregnancy.

Perioperative care including management of complications

Positioning during surgery

In order to avoid an aortocaval compression syndrome, it is recommended to routinely place the patient in the left lateral position (8). There are neither RCTs nor case series addressing this issue; the recommendation is based on the clinical experience of operating teams. While compression of the vena cava can lead to reduced venous return and hypotension in the mother, partial compression of the aorta when the mother is in the supine position is even more dangerous for the fetus than the mother, because the mother's arterial blood pressure may remain stable even though arterial hypotension is found in the uterine artery. Depending on the position of the fetus, employing a right lateral position or close monitoring with prompt corrective measures (expanding volume, medications) can improve the hemodynamic status.

During laparoscopic surgery a steep head-down position is often needed. When the uterus is enlarged as in pregnancy or when the adnexal structures are difficult to visualize, it may help to employ a head-down lateral positioning which improves the view of the contralateral adnexal structures. The anesthetic aspects of a head-down positioning are discussed below.

Intra-abdominal pressure / alterations in acid-base status

The US guidelines recommend a pneumoperitoneal pressure of <15 mm Hg. This helps reduce uteroplacental hypoperfusion and maternal cardiac overload, as well as to reduce the increase in pCO_2 during capnoperitoneum (19–21).

When creating the CO_2 -pneumoperitoneum (capnoperitoneum), one generally notices an increase in the arterial CO_2 partial pressure (pCO_2) which is primarily caused by increased trans-peritoneal absorption of CO_2 . If this increase is unrecognized, it can lead to hypercapnia and respiratory acidosis which in turn may cause stimulation of the sympathetic nervous system and cardiac arrhythmias, as well as fetal acidosis (22). Therefore, during laparoscopy measuring the end expiratory CO_2 levels (capnometry) should be routine, with the ventilation adjusted to the CO_2 levels (8, 20, 21,

BOX 1

Indications (and limitations) for laparoscopy during pregnancy

● Indications

- Acute appendicitis
- Cholelithiasis/cholecystitis
- Acute abdomen, etiology unclear
- Adnexal torsion/tumor
- Symptomatic myoma
- Symptomatic ovarian cyst
- Pelvic lymph node dissection, such as for cervical carcinoma (combined, for example, with radical vaginal trachelectomy)

● Limitations

- Diffuse peritonitis for example with appendicitis
- Advanced pregnancy with markedly enlarged uterus
- Lack of experience of the surgeon or operating team

23–26). If the maternal history or peripartum complications raise the suspicion of possible gas exchange abnormalities, then there should be no hesitancy in employing perioperative arterial paO_2 monitoring (8).

Respiratory problems

A clear increase in oxygen consumption and a simultaneous reduction in the functional residual capacity and thus in the oxygen reserve mean that during the induction and maintenance of anesthesia in a pregnant women, a critical hypoxemia can develop, especially when positioning or use of a capnoperitoneum leads to a dislocation of the endotracheal tube or a reduction in respiratory compliance. During laparoscopy in particular, a correctly placed endotracheal tube may be accidentally displaced by the head-down positioning and the increased intra-abdominal pressure and wind up in the right main bronchus, resulting in unilateral ventilation (22, 27). After each change in the patient's position, auscultation should be used to confirm the correct position of the endotracheal tube.

Miscarriages and preterm births

Although there is no increase in the fetal malformation rate following surgical procedures under general anesthesia, studies indicate that there is a slight increase in the miscarriage rate (28, 29). It is unclear if the surgical procedure or the anesthesia is responsible. Brodsky et al. (28) compared 187 women who had a surgical procedure under anesthesia in the first trimester to a control group of 8654 pregnant woman; they found a miscarriage rate that was significantly higher than that in controls (8.0% versus 5.1%) (2nd trimester 6.5% versus 1.4%). The largest published study is that of Mazze and Källén which includes 720 000 pregnant

TABLE 2

Miscarriage and preterm birth rates for appendectomies

Study	Year	Surgical indication	Laparoscopies (n)	Laparotomies (n)	Miscarriage rate after laparoscopy (%)	Miscarriage rate after laparotomy (%)	Preterm birth rate after laparoscopy (%)	Preterm birth rate after laparotomy (%)
Erekson et al. (3)	2012	Abdominal surgery (44% appendectomy)	986	535	No data	No data	No data	No data
Corneille et al. (e25)	2010	Appendectomy	9	40	0	7.5	11.1	12.5
Sadot et al. (e26)	2010	Appendectomy	41	16	2.4	0	29.2	18.7
Kirshtein et al. (e27)	2009	Appendectomy	23	19	4.3	5.2	No data	No data
McGory et al. (4)	2007	Appendectomy	454	2679	6.8	3.2	No data	No data
Upadhyay et al. (e28)	2007	Appendectomy	4	2	0	0	25	0
Carver et al. (e29)	2005	Appendectomy	17	11	11.7	0	11.7	0
Lyass et al. (e30)	2001	Appendectomy	11	11	0	0	0	0
Affleck et al. (20)	1999	Appendectomy	19	18	0	0	15.7	11.1
Conron et al. (e31)	1999	Appendectomy	12	9	0	0	No data	No data
Gurbuz et al. (e32)	1997	Appendectomy	5	4	0	0	0	0
Curet et al. (30)	1996	Appendectomy	4	7	0	0	No data	No data
Amos et al. (e33)	1996	Appendectomy	3		No data		No data	
Andreoli et al. (12)	1999	Appendectomy	5		0		0	
Barnes et al. (e34)	2004	Appendectomy	2		0		0	
Buser et al. (e35)	2002	Appendectomy	1		0		0	
dePerrot et al. (e36)	2000	Appendectomy	6		33.3		16.6	
Friedman et al. (e37)	2002	Appendectomy	1		100		0	
Geisler et al. (e38)	1998	Appendectomy	2		0		0	
Halkic et al. (e39)	2006	Appendectomy	11		0		0	
Hee et al. (e40)	1999	Appendectomy	7		No data		No data	
Lemaire et al. (e41)	1997	Appendectomy	4		0		0	
Moreno-Sanz et al. (e42)	2007	Appendectomy	6		0		16.6	
Palanivelu et al. (e43)	2006	Appendectomy	7		0		0	
Posta et al. (e44)	1995	Appendectomy	1		0		0	

Study	Year	Surgical indication	Laparoscopies (n)	Laparotomies (n)	Miscarriage rate after laparoscopy (%)	Miscarriage rate after laparotomy (%)	Preterm birth rate after laparoscopy (%)	Preterm birth rate after laparotomy (%)
Radwan et al. (e45)	2007	Appendectomy	1		0		0	
Rizzo et al. (e46)	2003	Appendectomy	4		0		0	
Rollins et al. (21)	2004	Appendectomy	28		0		21.4	
Schwarzberg et al. (e47)	1997	Appendectomy	1		0		0	
Thomas et al. (e48)	1998	Appendectomy	2		0		50	
Tracey et al. (e49)	2000	Appendectomy	3		0		No data	
Wu et al. (e50)	2005	Appendectomy	11		27.2		0	
Schmidt et al. (e5)	2007	Appendectomy	15		0		13.3	

BOX 2

Additional indications and surgical approaches

● Symptomatic ovarian cysts

- Randomized controlled studies addressing the optimal surgical approach are not available; a Cochrane analysis of available case series confirmed the advantages and disadvantages of laparoscopy versus laparotomy (e6).

● Adnexal torsion

- Women with adnexal pain suggesting torsion should be evaluated with laparoscopy, whether pregnant or not, in order to avoid organ loss (8, e7, e8).

● Enucleation of myoma

- Myoma enucleation during pregnancy (2.1% require therapy [e9]) are usually treated via laparotomy but there are case reports about successful laparoscopic enucleation (e10, e11).

● Oncologic surgery

- Oncologic abdominal procedures during pregnancy are associated with more morbidity than the above-described procedures (e12). Laparoscopic lymph node dissection for cervical carcinoma is safe from an oncological point of view and can be performed without complications (e13, e14).

women including 5405 who underwent surgery with anesthesia. The number of children with a reduced birth weight was increased, both because of intrauterine growth retardation as well as an increase in preterm births. This study failed to identify any specific surgical and anesthetic approach as associated with worse results.

A letter survey of laparoscopic surgeons revealed that in 413 laparoscopic procedures during pregnancy there were only 15 cases with perioperative complications (11). Reedy et al. in Sweden studied two million pregnancies over a period of 20 years (10). Their collective included 2181 laparoscopies and 1522 laparotomies (4–20 weeks of gestation). Preterm births, developmental problems, and reduced birth weight were much more common in children of operated mothers than children whose mothers had not undergone surgery, supporting other studies. However, no differences were found between patients undergoing laparoscopy versus laparotomy.

There are numerous studies that indicate fetal advantages of laparoscopy over laparotomy in pregnancy. But the data on miscarriages and preterm births is contradictory, as seen in the meta-analyses discussed in the section on appendectomy which show a significantly increased rate of miscarriages with laparoscopy but no significant differences in preterm birth rates (6,7, 30) (*Table 2*).

Fetal monitoring

The fetal and uterine status should be followed as in the US guidelines after the 16th week of pregnancy with both pre- and post-operative monitoring and documentation (8). Intra-operative monitoring does not improve the mortality (14, 20, 21, 31). Monitoring makes it possible to identify fetal problems early and institute measures to improve uterine perfusion (correction of hypoxemia, increasing blood pressure, re-positioning). When evaluating the fetus, one must remember that under general anesthesia the fetus is also anesthetized. Cardiotocography (CTG) or electronic fetal monitoring may reveal a marked reduced variability in fetal heart rate and oscillation which can be mistaken for an adverse cardiac event by individuals not familiar with the phenomenon. The reduced variability may persist post-operatively as the half-life of many anesthetics is longer in the fetus. An obstetrician should always be involved perioperatively. Postoperatively depending on the week of gestation either electronic fetal monitoring or sonography may be useful.

Tocolytic agents

Intra-abdominal procedures may lead to manipulation and displacement of the uterus which often leads to premature contractions (32). No study has identified an influence of anesthesia or given anesthetic agents on the frequency of preterm births (32). Some of the anesthetic agents, including many of the inhaled agents, are potent inhibitors of uterine contraction.

Although tocolytics like indomethacin suppositories (33) have no influence on anesthesia, beta-mimetic agents can have circulatory effects in the mother and cross-react or even potentiate drugs used during anesthesia (34). In the post-operative period, the combination of wound pain and administration of analgesic agents makes it difficult to identify premature contractions. The US guidelines recommend tocolytic therapy if premature contractions are identified (35–37). Prolonged use of tocolytic agents for more than 48 hours is not recommended for routine clinical practice (34).

Antibiotics, lung maturity and Rh prophylaxis

Antibiotics should be chosen depending on the indications for the planned operation, following the same recommendations as if the patient was not pregnant; however, teratogenic antibiotics should be avoided. If the clinical situation allows it, respiratory distress syndrome prophylaxis (pharmacological stimulation of fetal lung maturity) should be considered, depending on the week of gestation.

In addition, the need for Rh prophylaxis should be evaluated. Even in the absence of visible intra-uterine bleeding, the manipulation of the pregnant uterus or adjacent organs during a procedure can lead to placental microtrauma or bleeding.

Surgical approach

Many studies report on the advantages of laparoscopy over laparotomy in pregnant women. These include reduction in the fetal respiratory depression because of less need for maternal postoperative analgesics (38–40, e1), fewer wound infections (39, e2, e3) and less manipulation of the uterus to obtain better visualization (e4). Additional advantages of laparoscopy include a shorter hospital stay and reduced risk of thromboembolic events (8). On the other hand, perforation of the uterus is one of the main risks of laparoscopy during pregnancy and is especially likely to occur as the trocar is introduced into the abdominal cavity (5). Accidental intrauterine insufflation with gas through a Veres needle increases the risk of preterm birth (11). Finally, laparoscopy is associated with a higher miscarriage rate than laparotomy, especially when employed for appendicitis (10), so that an open approach should be chosen in this clinical situation in order to maximize fetal safety.

The localization of the trocar is crucial for the laparoscopic surgeon in order to minimize the risk of injuring the uterus. The site of trocar placement depends on the size of the uterus as well as the planned operation and the preferences of the surgeon (e5).

Risk of aspiration/ anesthesia

Additional practical guidance on reducing the risk of aspiration as well as on the use of inhalation and intravenous anesthetics during pregnancy can be found in the *eBox*.

KEY MESSAGES

- About 2% of pregnant women require a non-obstetric operation during pregnancy; the most common operation is appendectomy, followed by cholecystectomy.
- The most important perioperative considerations for the surgeon and anesthetist are: safety of the mother, safety of the fetus, avoiding teratogenic medications, and avoiding fetal acidosis and hypoxemia, as well as preventing preterm birth.
- Meta-analyses have shown that a laparoscopic appendectomy leads to significantly more miscarriages than an open procedure.
- If the indications for a surgical procedure are present, then one can operate during each trimester without increasing the risk for the mother or the fetus.
- Surgery during pregnancy should ideally be performed in centers that have interdisciplinary experience in the surgical management of pregnant patients and where even in non-obstetric procedures, an obstetrician and a neonatologist are readily available.

Conflict of interest statement

The authors declare that no conflicts of interest exist.

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REVIEW ARTICLE

Abdominal Surgery in Pregnancy—an Interdisciplinary Challenge

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eBOX

Risk of Aspiration

The mechanical effects of the enlarged uterus, decreased tone of the lower esophageal sphincter and increased gastric acid secretion (e16) all lead to an increased risk of aspiration in pregnant patients undergoing general anesthesia. In addition, during laparoscopy, the creation of a capnoperitoneum increases the intraabdominal pressure and thus the risk of regurgitation (e17). The Mendelson syndrome—the occurrence of aspiration pneumonia following aspiration of gastric acid or acidic gastric contents—poses another danger for pregnant patients (e18). Therefore endotracheal intubation with continuous cuff pressure monitoring for aspiration prophylaxis is the gold standard for managing the airway in patients after the 12th week of gestation (27), even though there are several case series supporting the safe use of a laryngeal mask for airway management in pregnant patients (e19).

The incidence of an unsuccessful intubation in pregnant patients is 1:280 versus 1:2330 in non-pregnant individuals and is the most common anesthetic cause of maternal death in Great Britain (e19). The causes include not only the physiologic changes during pregnancy (increased perfusion and swelling of the mucosa, increased breast volume, reduced neck mobility, tendency to hypoxia because of a 20% reduction in functional residual capacity, flatter positioning of ribs, cranial shift of diaphragm, increase in oxygen consumption by 20%) (e20), but also frequently insufficient depth of anesthesia and muscle relaxation. Therefore every facility should establish an algorithm for managing difficult airways in pregnant patients and practice the use of this algorithm regularly.

Anesthesia

Since laparoscopic surgery always requires general anesthesia, we will not further explore the differences between regional and general anesthesia. But we emphasize that there are no studies showing an advantage to regional anesthesia over general anesthesia in pregnancy. Supplemental regional anesthesia during general anesthesia can and should be employed in pregnant patients following the well-accepted recommendations for non-pregnant patients.

All of the standard inhalation and intravenous anesthetics as well as supplementation with opioids and muscle relaxants are suitable for pregnant patients. An increased miscarriage rate has not been found for any anesthetic. Propofol can be used during the entire pregnancy for the induction and maintenance of anesthesia. No teratogenic risk has been identified, although systemic studies have not been carried out. One must also emphasize that the use of propofol during pregnancy constitutes „off label use“. Because of a possible increased risk of cleft lip and cleft palate, as well as cardiac malformations, benzodiazepines should be avoided, especially in the 1st trimester.

Even though rodent studies have shown teratogenic effects from inhalation anesthesia when the animals have been exposed for several hours on different days, one can still be confident that inhalation anesthesia (enflurane, isoflurane, sevoflurane, desflurane) has no teratogenic effects when used during pregnancy. Even if these animal studies are relevant for humans, then they are more important for operating room personnel than for patients, as the patients do not have prolonged exposure to inhalation anesthetics. Even though pregnant and nursing operating room personnel are regularly exposed to inhalation anesthetic agents, the Professional Association of German Anesthetists (BDA, Berufsverband Deutscher Anästhesisten) in their recommendations for work place safety in the operating room state that there is no risk to pregnant or nursing personnel from the usual anesthetic gases (not including halothane and N₂O) as long as the allowable concentration levels are observed, monitoring for leakage is continuous and the recommendations of the Institute for Occupational Safety and Health (IFA, Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung) BG/BIA 1017 are followed (e21).

Nonetheless, when using volatile anesthetics, one must be aware that they reduce uterine tone in a dose-related manner and thus should not be administered in higher concentrations, especially since the minimum alveolar concentration (MAC) is reduced by 30–40% in pregnancy.

Some studies have demonstrated increased neuronal apoptosis and impaired synaptogenesis in the brains of immature rodents exposed to anesthetics (e22); these changes lead to abnormal behavior patterns. However, since the nature and the duration of synaptogenesis are completely different in humans and rodents, one cannot extrapolate this animal data to humans (e23).

The largest meta-analysis addressing this issue included 12 452 patients and found no increase in significant malformations. This same study showed that general anesthesia was not an independent risk factor for miscarriage when used for surgical procedures in pregnant women (e24).