

Expert Review of **Obstetrics & Gynecology**

EDITORIALS

Fetal androgen excess provides a developmental origin for PCOS

Uterine cervix defense mechanism against infection and preterm birth

KEY PAPER EVALUATION

A serum biomarker panel including kallikreins to predict ovarian cancer

REVIEWS

Prenatal gene therapy for the early treatment of genetic disorders

Magnetocardiography in the assessment of fetal arrhythmias

Laparoscopic management of pelvic pathology during pregnancy

Microanatomy and function of the eutopic endometrium in endometriosis

Microarray-based comparative genomic hybridization in prenatal diagnosis

Laparoscopic management of pelvic pathology during pregnancy

Expert Rev. Obstet. Gynecol. 4(1), 53–60 (2009)

Linda M Nicoll and
Camran Nezhat*

*Author for correspondence
Center for Special Minimally
Invasive Surgery, 900 Welch
Road, Suite 403, Stanford
University Medical Center,
Palo Alto, CA 94304, USA
Tel.: +1 650 327 8778
Fax: +1 650 327 2794
cnezhat@stanford.edu

The following article presents an overview of current practices in laparoscopy for pelvic pathology during pregnancy. It includes a review of physiologic changes in pregnancy. Common indications for surgery during pregnancy, including adnexal masses, appendicitis and biliary disease are discussed. Recommendations for the safe practice of laparoscopy in pregnancy including timing and operative techniques are provided.

KEYWORDS: adnexa • appendectomy • cholecystectomy • laparoscopy • malignancy • ovary • pregnancy

Nonobstetric surgery is performed in 1.6–2.2% of pregnant women, comprising approximately 50,000 cases per year in the USA [1]. Operative laparoscopy is becoming increasingly popular owing to the low postoperative morbidity and minimally invasive nature of procedures [2]. It has been associated with more rapid return of bowel function, decreased postoperative incisional pain, reduced requirement for pain medications and lower morbidity from atelectasis and thromboembolic events [1]. It is therefore not surprising that the laparoscopic approach in the pregnant patient is gaining acceptance as the method of choice for treating a variety of conditions, including adnexal masses, heterotopic pregnancy, appendicitis and cholecystitis. Additional indications for laparoscopic surgery in pregnancy have included adrenal tumors, splenic and renal disorders and abdominal pain of unknown etiology [3]. However, concern exists for the specific challenges of performing surgery on the pregnant patient. Namely, the effects of anesthesia, pneumoperitoneum, instrumentation and positioning must be carefully considered. This article reviews current indications and recommendations for laparoscopy in the pregnant patient.

Surgical indications

Surgery for adnexal masses

Adnexal masses are reported to occur in between one in every 81–2500 live births, with an average of one in 600. Only between 1 and 8% of adnexal masses in pregnancy are found to be malignant [1,4]. Most are benign with an anechoic,

simple cyst (which carries the least risk of being malignant) being the most common finding [6,7]. Among all adnexal masses in pregnancy, 30% are found to represent corpus luteum and between 24 and 40% represent benign cystic teratomas or dermoid cysts [8]. However, adnexal tumors greater than 5–6 cm are considered significant in both the pregnant and nonpregnant state and a general consensus exists that masses that persist beyond 15–16 weeks require a tissue diagnosis [1]. Traditional management has been to follow conservatively until 15–16 weeks' gestation and then to remove any adnexal masses greater than this size [1].

Conservative observation of benign pathology has been associated with complications 13–42% of the time [1]. There is literature on women with adnexal masses followed expectantly during pregnancy dating from 1906, a time when surgery was a considerably more perilous undertaking than it is at present [9]. Surgical mortality in these early years was as low as 4.6%, compared with a mortality rate of 26% in women followed expectantly. Deaths were attributed to suppuration of adnexal torsion, hemorrhage or peritonitis and sepsis from ruptured cysts or obstruction of labor. Later studies noted that 80% of cysts causing serious complications in patients managed expectantly were greater than 6 cm in diameter [10].

In 1984, in a series of 90 cases with adnexal tumors greater than 5 cm in diameter, Struyk reported that of the 75 tumors not removed electively at the time of diagnosis, 13 (17%) required emergency surgery prior to 16 weeks [11]. Of the

remaining 62 patients who were managed expectantly, two (3.2%) had torsion, with one resulting in preterm labor and neonatal death at 24 weeks. In total, 13 (20%) of these patients had obstruction at parturition and six (9.5%) had cyst rupture during labor with ensuing peritonitis and postpartum sepsis. In general, surgical intervention even in asymptomatic patients may be justified if the incidence of potential complications without surgery is high and an adverse effect on the pregnancy can be reasonably expected [1].

Although ovarian malignancy is rarely diagnosed in pregnant patients because of the young age of the reproductive demographic, 1–8% of adnexal masses in pregnancy have been observed to be malignant [1,4,5]. Given the fact that survival in ovarian cancer is largely dependent upon the stage at which the disease is diagnosed, removal of persistent adnexal masses (especially those with features suggestive of malignancy on ultrasound, color Doppler or magnetic resonance imaging) should be undertaken even during pregnancy so as to avoid an unnecessary delay in diagnosis and treatment. The role of maternal hormone secretion in accelerating the growth of hormone-dependent tumors also argues for prompt removal of a suspicious adnexal mass. Although both transcutaneous and transvaginal aspiration have been suggested and attempted as alternatives to removal, several reports in the literature demonstrate diffuse intra-abdominal dissemination of ovarian cancer after cyst aspiration [12,13].

Waiting until 15–16 weeks' gestation allows for the majority of cysts that are likely to regress to do so spontaneously [11,14], for the fetus to complete organogenesis and for most of the spontaneous miscarriages that are expected to have already taken place [1]. However, unequivocal indications for surgical intervention in the first trimester do exist and operative laparoscopy in early pregnancy has been found to be both safe and feasible [14,15]. In a series of 11 patients undergoing laparoscopic surgery during the first trimester, the indications for surgery included persistent and enlarging ovarian cysts, torsion of adnexa and rupture of cysts with internal bleeding [16].

Appendectomy

Appendicitis is the most common acute general surgical condition during pregnancy [17]. Approximately 0.05–0.1% of pregnant women will have appendicitis, which is evenly distributed through all three trimesters [18,19]. Appendicitis in pregnancy presents a unique diagnostic challenge due to the anatomic and physiologic changes discussed previously. There is also an effect of advancing gestation in making the correct diagnosis. The preoperative diagnosis of appendicitis is correct in the first trimester 85% of the time, but only correct 30–50% of the time in the second and third trimesters [18].

Risk of complications, including spontaneous miscarriage and preterm labor, increases greatly with perforation [20–24]. It is owing to the morbidity of appendiceal perforation that, in routine surgical treatment of appendicitis, a one-third false-positive rate is generally considered acceptable [24–26].

Laparoscopy offers the ability to allow the surgeon to diagnose pathology more accurately in a less-invasive manner than laparotomy. With increasing acceptance of laparoscopic appendectomy

in pregnancy, risk of fetal mortality may decrease as surgeons' hesitancy to offer surgical intervention lessens. It is therefore recommended that the pregnant patient with acute appendicitis be treated in a manner identical to the nonpregnant patient with regard to rapid resuscitation with intravenous fluids, antibiotics and prompt surgical intervention.

Cholecystectomy

Pregnancy predisposes women to the formation of gallstones. While gallstones can be found in 4.5–12% of all pregnant patients, only 0.05% will suffer symptomatic cholelithiasis [27]; 40% of these patients will require cholecystectomy. This makes cholecystectomy the most common general surgical procedure in pregnancy, with three to eight out of 10,000 pregnancies requiring the procedure [18].

Until recent years, cholecystectomy in pregnancy was traditionally managed conservatively [24]. The case for more-aggressive management was greatly aided by a 1987 review of 44 patients with biliary colic [28]. Of the 26 patients managed conservatively, 58% had recurrent episodes of colic, with some requiring parenteral nutrition and one developing pancreatitis; three (12%) suffered spontaneous miscarriage. Of the 18 patients who underwent laparotomy for gallbladder removal, none miscarried. All of the patients available for follow-up delivered at term, except for one patient who delivered at 8 months' gestation after a diagnosis of preeclampsia.

As in the case of appendicitis, delay in diagnosis and treatment of biliary disease carries serious risks for both the mother and fetus. Nonoperative management of symptomatic cholelithiasis increases the risk of gallstone pancreatitis by up to 13% [29]. This complication carries a 15% risk of maternal mortality [18–27]. Moreover, while only 5% of patients undergoing uncomplicated cholecystectomies suffer pregnancy loss, this rate is as high as 60% in cases complicated by gallstone pancreatitis [19].

Initial management of symptomatic cholelithiasis should be the same as in the nonpregnant patient. Restriction of oral intake, intravenous hydration and analgesic support should be accompanied by antibiotic therapy as needed [27,30]. The risk of relapse after conservative therapy is greatest in the first trimester, at 92%. The risk decreases to 64% in the second trimester and 44% in the third [27].

Owing to the location of the gallbladder in the right upper quadrant, laparoscopic cholecystectomy appears feasible even at an advanced gestational age [1]. Improved outcomes with decreased risk of spontaneous abortion and preterm labor have been reported with a laparoscopic approach compared with laparotomy [27]. The indications for surgery include failed medical therapy, obstructive jaundice, gallstone pancreatitis and peritonitis [30]. The indications for operative cholangiography are also identical to those in the nonpregnant patient. They include a total bilirubin of 1.5 ng/dl or greater, a dilated common bile duct 8 mm or greater and the presence of gallstone pancreatitis [19]. When cholangiography is used, a lead abdominal shield may be employed to minimize risk to the fetus [2].

Solid organ resection

Laparoscopic adrenalectomy during pregnancy has been successful in the treatment of primary hyperaldosteronism [31], Cushing's syndrome [32-34] and pheochromocytoma [35-40]. Laparoscopic splenectomy has been used in the management of antiphospholipid syndrome [41], hereditary spherocytosis [42] and autoimmune thrombocytopenia purpura [43-45] in pregnant patients with excellent outcomes for mother and fetus. Two cases of laparoscopic nephrectomy in the first [46,47] and one in the second [48] trimester of pregnancy have been reported without adverse events for the mother or fetus.

Laparoscopic myomectomy

The literature includes a few isolated case reports of laparoscopic myomectomy performed in the second trimester of pregnancy [49,50]. This type of procedure can be undertaken in carefully selected patients with acute abdominal pain. It remains, however, experimental and somewhat controversial.

Pregnancy outcomes & fetal risk

Risk to the fetus

Limited reports suggest that surgery during pregnancy may be associated with a greater risk of pregnancy loss or premature labor [1]. Evidence suggests that intra-abdominal procedures and those requiring cervical manipulation were associated with a greater tendency for premature labor than extra-abdominal procedures [51,52]. However, the question remains as to whether the increased risk of premature labor is due to the surgery or to the condition itself requiring surgical intervention.

The clearest example of this is in the case of appendicitis, where perforation of the appendix is associated with at least a four-times higher risk of preterm labor than nonperforated appendicitis [20-24]. Fever and pyrexia themselves may induce uterine contractions [25]. It is therefore reasonable to posit that inflammation and infectious processes themselves may increase the risk of pregnancy loss and preterm delivery, rather than surgery itself [1].

Surgery undertaken in the third trimester and surgery that is performed emergently as opposed to electively have a higher risk of spontaneous miscarriage and preterm labor. In a review of 55 cases of adnexal masses in pregnancy [53], Hess noted no pregnancy losses in the 39 patients who underwent elective surgery for removal. Of the six cases undergoing emergent surgery in the first trimester, three (50%) suffered spontaneous miscarriage. Only one of eight patients undergoing emergent removal between 12 and 30 weeks had a pregnancy loss. On the other hand, of the two patients undergoing emergency surgery for torsion and rupture after 31 weeks, both experienced preterm delivery within 72 h.

Therefore, it is reasonable to say that surgery itself may not present a risk to the pregnancy if performed in a nonemergent setting, preferably in the second trimester and if uterine and cervical manipulation can be avoided [1].

The risk of fetal acidosis due to the use of CO₂ pneumoperitoneum has been studied in animal models with conflicting results. Although some animal studies have confirmed fetal acidosis with associated tachycardia, hypertension and hypercapnia during

CO₂ pneumoperitoneum [54-56], other animal studies have demonstrated no fetal acidosis [57]. More importantly, no long-term adverse effects have been identified in these studies [54-57]. Fetal acidosis with insufflation has not been documented in the human fetus. Therefore, the most effective strategy for ensuring adequate oxygenation of the fetus, it would seem, is to ensure close monitoring and adequate oxygenation of the mother.

Long-term follow-up

Laparoscopy has been safely performed in all trimesters of pregnancy with good fetal and maternal outcomes. However, the long-term effects to the child after delivery have not been well studied. One recent study evaluating 11 children from aged 1-8 years whose mothers underwent laparoscopic surgery while pregnant did not find any growth or developmental delays [17].

Physiologic changes & maternal risk

Physiologic changes in pregnancy

Physiologic changes in pregnancy must be taken into account when discussing surgery in this group of patients. Respiratory changes include an increase in minute volume up and a mild respiratory alkalosis [58]. Cardiovascular changes include mild anemia, increased cardiac output, increased heart rate and increased oxygen consumption. Altered gastric motility contributes to gastroesophageal reflux, which can increase the risk of aspiration. These changes must be taken into account when monitoring the patient under general anesthesia.

Changes in the circulatory system, which include a significant increase in blood volume diverted to the growing uterus and feto-placental unit, must also be taken into account when considering pelvic surgery. The engorged uterus may be prone to excessive bleeding when traumatized. It is for this reason that, in general, uterine surgery should be deferred during pregnancy whenever possible.

Altered physiology also contributes to an increased risk of perioperative thromboembolic disease. A mildly thrombogenic state in these patients is the result of increased fibrinogen, factor VII and XII and decreased levels of antithrombin III. There is a paucity of research on prophylaxis for deep venous thrombosis in the pregnant patient in general and no data exist regarding the use of unfractionated or low-molecular-weight heparin for prophylaxis in pregnant patients undergoing laparoscopy [3]. Increased vigilance for venous thromboembolism and conscientious employment of preventive measures (including antiembolism stockings, pneumatic compression devices and early ambulation) are the best strategies available in preventing this devastating complication.

Last, and significantly, the diagnosis of abdominal pathology in pregnancy can be complicated by changes in anatomy and symptomatology. The usual location of abdominal organs is changed when they are pushed cephalad by the gravid uterus. Nausea and vomiting as well as leukocytosis, lowgrade fever, anorexia and mild hypotension are common and cannot be relied upon in assessing the acute abdomen as they are in the nonpregnant patient. To some degree, the surgeon must rely on other tools in his or her diagnostic arsenal for these patients.

Effects of pneumoperitoneum on maternal physiology

The creation of pneumoperitoneum can have a deleterious effect on maternal acid–base status and hemodynamics, which might pose a threat to the fetus. Insufflation of the peritoneal cavity has two immediate effects. First, it increases the intra-abdominal pressure, displacing the patient's diaphragm. This results in decreased residual lung volume and functional residual capacity, predisposing the patient to arterial oxygen desaturation [59]. Second, the induction of CO₂ pneumoperitoneum induces a gaseous exchange leading to an equilibrium with gases in the blood. It is therefore of concern as to whether the induction of pneumoperitoneum might lead to possible acid–base imbalance from CO₂ absorption and hypercarbia [60]. CO₂ is absorbed across the peritoneal surface and equilibrates into the bloodstream, eventually making its way into muscle, viscera and even bone. Patients undergoing a long laparoscopic procedure are at risk of maintaining hypercarbia and acidosis postoperatively until all excess CO₂ is eliminated from the tissues.

Monitoring end-tidal CO₂ is useful so that, when a rise is detected, controlled hyperventilation of the patient can be used to eliminate excess CO₂ via the alveoli. A reasonable goal may be set at less than 35 mmHg [2]. However, a mismatch in ventilation in relation to perfusion can lead to falsely normal or low end-tidal CO₂ readings. Monitoring of arterial partial pressure of CO₂ may be preferable for some patients with medical comorbidities in order to limit the risk of hypercarbia and acidosis from compromised cardiopulmonary status. Close monitoring of arterial partial pressure of CO₂ can also be important to minimize the decrease in cardiac output that results from the effect of CO₂ in increasing mean arterial pressure and total peripheral resistance.

Hemodynamic effects of pneumoperitoneum also contribute to a reduction in cardiac output as a result of direct alteration of venous resistance in the inferior vena cava and decreased mean systemic pressure [61]. This is of particular concern during and after the second trimester, when pressure from the enlarged uterus on the vena cava already decreases venous return. It is for this reason that slight lateral positioning of the mother is recommended at the time of surgery [1,16]. This deviation from the usual practice of patient positioning should be taken into account at the time of trocar placement, when the relationship of anatomic landmarks to underlying structures may be affected.

Increased intra-abdominal pressure causing decreased venous return and cardiac output may contribute to decreased uterine and fetal perfusion. This decrease is volume-dependent. Therefore, in an adequately resuscitated pregnant woman, increased intra-abdominal pressure should not lead to decreased CO₂ and fetal blood flow [62].

The use of low-pressure pneumoperitoneum has been suggested following the entry phase of laparoscopy, with a maximum of 8–12 mmHg, so as to minimize any adverse effect on fetal perfusion [2]. However, others have argued that insufflation less than 12 mmHg may not provide adequate visualization of the intra-abdominal cavity [29,63]. Pressures up to 15 mmHg have been used during laparoscopy on pregnant patients without increasing adverse outcomes for the patient or the fetus [29,63].

Concerns related to the effects of pneumoperitoneum on the mother and fetus have led to the development of techniques using abdominal wall elevators in 'gasless' or 'isobaric' laparoscopy. There are reports in the literature of the successful use of gasless laparoscopy during pregnancy [49,64–70] but this technique is not used widely and has not been evaluated systematically for safety compared with conventional laparoscopy.

Technique

Anesthetic considerations

General anesthesia with curarization and endotracheal intubation is essential for safely performing laparoscopy [15]. The majority of anesthetic drugs, skeletal muscle relaxants and morphine-related drugs are nonteratogenic and nontoxic for the fetus [71]. They can be used for surgery during pregnancy where indicated.

The patient should be placed in the left lateral recumbent position (or in the lithotomy position with a left tilt) to reduce compression of the vena cava and subsequent reduction in venous blood return to the heart [1,3,16]. Change in position to Trendelenburg should be undertaken slowly [15,16] so as to minimize the hemodynamic effects of a sudden increase in venous return from the relatively blood-enriched pelvic area.

A nasogastric or orogastric tube is recommended in pregnant patients (and in all patients undergoing laparoscopy) to decrease the risk of stomach injury and to minimize the risk of aspiration of gastric contents.

Entry techniques

With enlarged uterine size, injury from Veress needle or trocar placement may occur. Risk of trocar injury to the uterus increases with increasing gestational age [58]. The first step in entry should involve palpation of the uterine fundus to help determine the optimal primary insertion site. During the first trimester, umbilical entry is safe. Later in pregnancy, sites in the midclavicular line (in the left or right upper quadrant), subxiphoid space or a supra-umbilical site may be used [1,72].

Both the Veress needle and open technique have been utilized safely and effectively. Some surgeons insert the Veress needle under ultrasound guidance in an effort to avoid underlying structures [16]. Pneumoamnion with pregnancy loss has been reported as a result of inadvertent uterine injury at the time of Veress needle placement [73]. To prevent this, the needle may be directed away from the gravid uterus (toward the upper abdomen) to decrease the likelihood of uterine injury [16]. Veress needle entry can be aided by the use of pneumoperitoneum creation assistance devices, such as the LapCap™ [74].

Some surgeons prefer the open method using the Hasson cannula owing to decreased theoretical risk to the uterus by avoiding blind entry [1]. Optical trocars have also been used [3] but the use of bladeless trocars in pregnancy has not been evaluated systematically. Surgeon preference is often the deciding factor in determining which method of entry is used. Regardless of the entry technique chosen, a Foley catheter should always be placed prior to abdominal entry to decrease risk of injury to the bladder and secondary trocars should be placed under direct observation.

It has been recommended that the maximum intra-abdominal pressure on the insufflator should be set at 15 mmHg [16], as opposed to the higher intra-abdominal pressures that are often employed during the entry phase in nonpregnant patients. This pressure may decrease following the entry phase to 8–12 mmHg [1] while paying attention to the maintenance of adequate visualization.

Uterine manipulation

Since instrumentation of the cervix is contraindicated, extra-corporeal uterine manipulation has been attempted, with some reported success [16]. Other recommendations that have been suggested include tilting the operating table away from the lesion and the use of smooth instruments to displace the uterus under direct visualization.

Electrosurgery & hemostasis

Bipolar cautery is recommended [15] for hemostasis to avoid 'sparking' phenomena associated with monopolar energy sources that may endanger the fetus or displaced bowel. It is fair to extrapolate that there may be an advantage in using tools that minimize the risk of thermal spread (i.e., tools with harmonic or radiofrequency technology), although this has never been studied formally. The use of the argon beam coagulator may be contraindicated, as this has been associated with reports of rapid overpressurization of the peritoneal cavity, resulting in gas embolism and death [75,76].

The potential danger of exposure to intra-abdominal smoke generated by electrosurgery and lasers, with increased production of noxious gases including carbon monoxide, remains unclear. However, no increase in the levels of carboxyhemoglobin have been detected in women undergoing prolonged operative laparoscopic procedures [77]. Nevertheless, rapid evacuation of intra-abdominal smoke is recommended.

The safety of adjunctive hemostatic medications and devices has often not been established in pregnancy. Their use should be avoided wherever possible.

Fetal surveillance

Surveillance of the fetal heart rate is recommended before and after surgery. Pre- and postoperative fetal heart activity should be documented. In high-risk patients, intraoperative transvaginal monitoring of the fetal heart rate is recommended as early as the second trimester [2]. In the event that fetal distress is detected, the surgeon can release the pneumoperitoneum and deflate the abdomen to potentially reverse the distress [2].

In viable gestations, a preoperative nonstress test is reasonable to reassure the surgeon of a healthy, well-oxygenated fetus. A nonreassuring preoperative nonstress test might be a contraindication to proceeding with any surgery and should be considered in its clinical context as a possible indicator for delivery of the fetus. A nonreassuring postoperative nonstress test should prompt expeditious evaluation of the mother to seek out and correct any reversible or physiologic causes, such as dehydration, undetected bleeding or maternal malpositioning.

A reasonable schedule of fetal surveillance should include an assessment in the immediate postoperative period, and might be followed by an assessment approximately 4 h later. Regular assessments in the postoperative days should follow [15].

Postoperative support

Some surgeons have recommended giving one dose of progesterone 50 mg intramuscularly after surgery for luteal support in patients at greater than 10 weeks' gestation. Patients less than 10 weeks received progesterone 200 mg orally twice daily until 10 weeks [16]. This was thought helpful in minimizing vaginal bleeding after surgery.

Tylenol alone has been used effectively for postoperative pain management in some patients [16], although other patients will require narcotic pain relief. Some surgeons have used ketoprofen as an analgesic and for the prevention of uterine contractions [15] in patients in the first and second trimester of pregnancy. There is, however, no evidence to support the routine use of prophylactic tocolytics [27]. In general, nonsteroidal anti-inflammatory agents are to be avoided after the second trimester, since their use is associated with an elevated risk of premature closure of the ductus arteriosus.

Expert commentary

Laparoscopic surgery in pregnancy is safe and feasible. It offers the patient the benefits of a minimally invasive approach, including decreased postoperative pain, decreased narcotic requirements, decreased recovery time, smaller incisions and a faster return to normal activity. The risks to the pregnancy appear smallest when surgery is performed in a nonemergent setting, in the second trimester and with careful monitoring of the special physiologic needs of the mother and fetus. Although current data are insufficient, there does not appear to be any long-term ill effects of laparoscopic surgery on either the mother or fetus.

It is not acceptable to delay treatment and diagnosis of surgical conditions in any patient owing to pregnancy status. In general, pregnant patients with an acute abdomen, appendicitis or cholecystitis should be treated in a manner identical to the nonpregnant patient with as little delay in surgical treatment as possible. Adnexal masses can be managed expectantly until they can be removed in the second trimester unless torsion, hemorrhage, suppurative, rapid enlargement or features suggesting malignancy are evident. Solid organ removal can be undertaken during pregnancy as medical circumstances dictate.

As laparoscopy in pregnancy becomes increasingly common and the surgeons' comfort level increases, prompt surgical intervention will prevent complications in the large number of patients with uncertain diagnoses and those who might otherwise be managed by previous conventional methods.

Five-year view

We expect that laparoscopic surgery will become the standard of care for a number of conditions encountered in pregnancy, just as it is currently the standard of care in the nonpregnant patient.

Eventually, laparotomy in pregnancy may become rare or obsolete as the benefits of a minimally invasive approach lead physicians to abandon older techniques.

As laparoscopy in pregnancy becomes more common for a wider variety of conditions, the literature will begin to focus less on isolated case reports of successful surgeries and should begin to focus on a systematic evaluation of the various techniques currently being employed. This shift will be important in developing an evidence-based best practice for fetal and maternal monitoring, primary entry techniques and the use of different energy modalities. This will improve safety and potentially increase the

number of surgeons who are capable of providing the benefits of a minimally invasive approach to their pregnant patients with surgical problems.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Key issues

Indications for and timing of laparoscopy in pregnancy:

- When possible, surgery should be undertaken:
 - Electively (in a non-emergent setting)
 - In the second trimester
- In an emergency setting, the pregnant patient with suspected intra-abdominal pathology should be treated in the same manner as a nonpregnant patient.
- Adnexal masses greater than 6 cm in diameter should be removed to reduce the risk of enlargement, torsion and rupture.
- Early diagnosis of malignant ovarian masses can improve patient outcomes.

Recommendations for laparoscopy in the pregnant patient include the following:

- Laparoscopy under general endotracheal anesthesia is generally considered safe in pregnancy.
- End-tidal CO₂ should be monitored, especially in high-risk patients.
- Care should be taken to minimize risk of venous thromboembolism.
- Changes in patient positioning (Trendelenburg and reverse) should occur slowly.
- Intra-abdominal pressure should be set at 15 mmHg during the entry phase and at no more than 12–15 mmHg during the operative phase of the procedure.
- Primary trocar placement depends on the height of the uterine fundus.
- Surgeon preference generally determines the mode of primary entry as both Veress and Hasson techniques have been used safely.
- Instrumentation of the cervix should be avoided.
- There is no evidence to support the routine use of prophylactic tocolytics.
- Fetal monitoring is recommended preoperatively and postoperatively. It can be accomplished safely intraoperatively when indicated.

References

Papers of special note have been highlighted as:

- of interest
 - of considerable interest
- 1 Nezhat FR, Tazuke S, Nezhat CH, Seidman DS, Phillips DR, Nezhat CR. Laparoscopy during pregnancy; a literature review. *JSLs* 1, 17–27 (1997).
 - Case series and thorough review of the literature regarding laparoscopy in pregnancy.
 - 2 Nezhat C, Nezhat F, Nezhat C. *Nezhat's Operative Gynecologic Laparoscopy and Hysteroscopy (3rd Edition)*. McGraw-Hill, NY, USA (2008).
 - Contains a chapter on laparoscopy in pregnancy detailing past experience and current recommendations from an expert laparoscopy practice.
 - 3 Jackson H, Granger S, Price R *et al*. Diagnosis and laparoscopic treatment of surgical diseases during pregnancy, an evidence-based review. *Surg. Endosc.* 22, 1917–1927 (2008).
 - Review of laparoscopy in pregnancy with a focus on general surgery and a helpful section on radiology.
 - 4 Peterson W, Prevost E, Edmunds F, Hundly J, Morris F. Benign cystic teratomas of the ovary: a clinico-statistical study of 1,007 cases with a review of the literature. *Am. J. Obstet. Gynecol.* 70, 368–382 (1964).
 - 5 Kort B, Katz VL, Watson WJ. The effect of non-obstetric operation during pregnancy. *Contracep. Fert. Sex.* 25, 375–379 (1997).
 - 6 Hogston P. Ultrasound study of ovarian cysts in pregnancy: prevalence and significance. *Br. J. Obstet. Gynecol.* 93, 625–628 (1986).
 - 7 Nelson MJ, Cavaliere R, Graham D, Sanders RC. Cysts in pregnancy discovered by sonography. *J. Clin. Ultrasound* 14, 509–512 (1986).
 - 8 Yuen PM, Chang AM. Laparoscopic management of adnexal masses during pregnancy. *Acta Obstet. Gynecol. Scand.* 76, 173–176 (1997).
 - 9 Patton CL. Ovarian cysts situated above the superior pelvic strait, complicated by pregnancy. *Surg. Gynecol. Obstet.* 3, 413–420 (1906).
 - 10 Grimes WH Jr, Bartholomew RA, Colvin ED, Fish JS, Lester WM. Ovarian cyst complicating pregnancy. *Am. J. Obstet. Gynecol.* 68, 594–603 (1954).
 - 11 Struyk APHB, Treffers PE. Ovarian tumors in pregnancy. *Acta Obstet. Gynecol. Scand.* 63, 421–424 (1984).

- 12 Trimbos JB, Hacker NF. The case against aspirating ovarian cysts. *Cancer* 72, 828–831 (1993).
- 13 de Crespigny L. A comparison of ovarian cyst aspirate cytology and histology: the case against aspiration of cystic pelvic masses. *Aust. NZ Obstet. Gynecol.* 35, 233–325 (1995).
- 14 Parker WH, Childers JM, Canis M, Phillips DR, Topel H. Laparoscopic management of benign cystic teratomas during pregnancy. *Am. J. Obstet. Gynecol.* 174, 1499–14501 (1996).
- 15 Mathevet P, Nezzah K, Dargent D, Mellier G. Laparoscopic management of adnexal masses in pregnancy, a case series. *Eur. J. Obstet. Gynecol. Reprod. Biol.* 108, 217–222 (2003).
- Case series with a useful review of the types of adnexal masses encountered in pregnant patients and their effective management via a minimally invasive approach.
- 16 Ko ML, Lai TH, Chen SC. Laparoscopic management of complicated adnexal masses in the first trimester of pregnancy. *Fertil. Steril.* DOI: 10.1016/j.fertnstert.2008.04.035 (2008) (Epub ahead of print).
- Case series of successful laparoscopies performed on pregnant patients. Contains detailed descriptions of useful techniques.
- 17 Rizzo AG. Laparoscopic surgery in pregnancy: long-term follow-up. *J. Laparoendosc. Adv. Surg. Tech. A* 13(1), 11–15 (2003).
- 18 Curet MJ. Special problems in laparoscopic surgery. Previous abdominal surgery, obesity, and pregnancy. *Surg. Clin. North Am.* 80, 1093–1110 (2000).
- 19 Gurbuz AT, Pectz ME. The acute abdomen in the pregnant patient. Is there a role for laparoscopy? *Surg. Endosc.* 11, 98–102 (1997).
- 20 Babakina A, Parsa H, Woodruff JD. Appendicitis during pregnancy. *Obstet. Gynecol.* 50, 40–44 (1977).
- 21 Bronstein E. Acute appendicitis in pregnancy. *Am. J. Obstet. Gynecol.* 86, 514 (1961).
- 22 Saunders P, Milton PJD. Laparotomy during pregnancy, an assessment of diagnostic accuracy of fetal wastage. *Br. Med. J.* 3, 165–167 (1973).
- 23 Shnider SM, Webster GM. Maternal and fetal hazards of surgery during pregnancy. *Am. J. Obstet. Gynecol.* 92, 891–900 (1965).
- 24 Sharp HT. Gastrointestinal surgical conditions during pregnancy. *Clin. Obstet. Gynecol.* 37, 306–315 (1994).
- 25 Ahlgren M. The influence of temperature on the motility of the human uterus *in vitro*. *Acta Obstet. Gynecol. Scand.* 38, 243 (1959).
- 26 Sarason EL, Bauman S. Acute appendicitis in pregnancy, difficulties in diagnosis. *Obstet. Gynecol.* 22, 382–386 (1963).
- 27 Graham G, Baxi L, Tharakan T. Laparoscopic cholecystectomy during pregnancy, a case series and review of the literature. *Obstet. Gynecol. Surv.* 9, 566–574 (1998).
- 28 Dixon NP, Faddis DM, Silberman H. Aggressive management of cholecystitis during pregnancy. *Am. J. Surg.* 154, 292–294 (1987).
- 29 Rollins MD, Chan KJ, Price RR. Laparoscopy for appendicitis and cholelithiasis during pregnancy. A new standard of care. *Surg. Endosc.* 8, 237–241 (2004).
- 30 Sen G, Nagabhushan JS, Joypaul V. Laparoscopic cholecystectomy in third trimester of pregnancy. *J. Obstet. Gynaecol.* 22, 556–557 (2002).
- 31 Shalhav AL, Landman J, Afane J, Levi R, Clayman RV. Laparoscopic adrenalectomy for primary hyperaldosteronism during pregnancy. *J. Laparoendosc. Adv. Surg. Tech. A* 10(3), 169–171 (2000).
- 32 Finkenstedt G, Gasser RW, Hofle G *et al.* Pheochromocytoma and sub-clinical Cushing's syndrome during pregnancy, diagnosis, medical pre-treatment and cure by laparoscopic unilateral adrenalectomy. *J. Endocrinol. Invest.* 22(7), 551–557 (1999).
- 33 Aishima M, Tanaka M, Haraoka M, Naito S. Retroperitoneal laparoscopic adrenalectomy in a pregnant woman with Cushing's syndrome. *J. Urol.* 164(3 Pt 1), 770–771 (2000).
- 34 Lo CY, Lo CM, Lam KY. Cushing's syndrome secondary to adrenal adenoma during pregnancy. *Surg. Endosc.* 16(1), 219–220 (2002).
- 35 Janetschek G, Finkenstedt G, Gasser R *et al.* Laparoscopic surgery for pheochromocytoma, adrenalectomy, partial resection, excision of paragangliomas. *J. Urol.* 160(2), 330–334 (1998).
- 36 Demeure MJ, Carlsen B, Traul D *et al.* Laparoscopic removal of a right adrenal pheochromocytoma in a pregnant woman. *J. Laparoendosc. Adv. Surg. Tech. A* 8(5), 315–319 (1998).
- 37 Pace DE, Chiasson PM, Schlachta CM, Mamazza J, Cadeddu MO, Poulin EC. Minimally invasive adrenalectomy for pheochromocytoma during pregnancy. *Surg. Laparosc. Endosc. Percutan. Tech.* 12(2), 122–125 (2002).
- 38 Gagner M, Breton G, Pharand D, Pomp A. Is laparoscopic adrenalectomy indicated for pheochromocytomas? *Surgery* 120(6), 1076–1080 (1996).
- 39 Wolf A, Goretzki PE, Rohrborn A *et al.* Pheochromocytoma during pregnancy, laparoscopic and conventional surgical treatment of two cases. *Exp. Clin. Endocrinol. Diabetes* 112(2), 98–101 (2004).
- 40 Kim PT, Kreisman SH, Vaughn R, Panton ON. Laparoscopic adrenalectomy from pheochromocytoma in pregnancy. *Can. J. Surg.* 49(1), 62–62 (2006).
- 41 Hardwick RH, Slade RR, Smith PA, Thompson MH. Laparoscopic splenectomy in pregnancy. *J. Laparoendosc. Adv. Surg. Tech. A* 9(5), 439–440 (1999).
- 42 Allran CF Jr, Weiss CA 3rd, Park AE. Urgent laparoscopic splenectomy in a morbidly obese pregnant woman: case report and literature review. *J. Laparoendosc. Adv. Surg. Tech. A* 12(6), 445–447 (2002).
- 43 Griffiths J, Sia W, Shaprio AM, Tataryn I, Turner AR. Laparoscopic splenectomy for the treatment of refractory immune thrombocytopenia in pregnancy. *J. Obstet. Gynaecol. Can.* 27(8), 771–774 (2005).
- 44 Iwase K, Higaki J, Yoon HE *et al.* Hand-assisted laparoscopic splenectomy for idiopathic thrombocytopenic purpura during pregnancy. *Surg. Laparosc. Endosc. Percutan. Tech.* 11(1), 53–56 (2001).
- 45 Anglin BV, Rutherford C, Ramus R, Lieser M, Jones DB. Immune thrombocytopenic purpura during pregnancy: laparoscopic treatment. *JSL* 5(1), 63–67 (2001).
- 46 O'Connor JPB, Biyani CS, Taylor J, Agarwal V, Curley PJ, Browning AJ. Laparoscopic nephrectomy for renal-cell carcinoma during pregnancy. *J. Endourol.* 18(9), 871–874 (2004).
- 47 Sainsbury DC, Dorkin TJ, MacPhail S, Soomro NA. Laparoscopic radical nephrectomy in first-trimester pregnancy. *Urology* 64(6), 1231 (2004).
- 48 Lee D, Abraham N. Laparoscopic radical nephrectomy during pregnancy: case report and review of the literature. *J. Endourol.* 22(3), 517–518 (2008).
- 49 Melgrati L, Damiani A, Franzoni G, Marziali M, Sesti F. Isobaric (gasless) laparoscopic myomectomy during pregnancy. *J. Minim. Invasive Gynecol.* 12(4), 379–381 (2005).

- 50 Pelosi MA, Pelosi MA, Giblin S. Laparoscopic removal of a 1500g syptomatic myoma during the second trimester of pregnancy. *J. Am. Assoc. Gynecol. Laparosc.* 2, 457-462 (1995).
- 51 Levine W, Diamond B. Surgical procedures during pregnancy. *Am. J. Obstet. Gynecol.* 81, 1046-1052 (1961).
- 52 Smith BE. Fetal prognosis after anesthesia during gestation. *Anesth. Analg.* 42, 521-526 (1963).
- 53 Hess LW, Peaceman A, O'Brien WF, Winkel CA, Cruikshank DP, Morrison JC. Adnexal mass occurring with intrauterine pregnancy: report of fifty-four patients requiring laparotomy for definitive management. *Am. J. Obstet. Gynecol.* 158, 1029-1034 (1988).
- 54 Hunter JG, Swanstrom L, Thornburg K. Carbon dioxide pneumoperitoneum induces fetal acidosis in a pregnant ewe model. *Surg. Endosc.* 9(3), 272-279 (1995).
- 55 Reedy MB, Galan HL, Bean-Lijewski JD, Carnes A, Knight AB, Kuehl TJ. Maternal and fetal effects of laparoscopic insufflation in the gravid baboon. *J. Am. Assoc. Gynecol. Laparosc.* 2(4), 399-406 (1995).
- 56 Curet MJ, Vogt DA, Schob O, Qualls C, Izquierdo LA, Zucker KA. Effects of CO₂ pneumoperitoneum in pregnant ewes. *J. Surg. Res.* 63(1), 339-344 (1996).
- 57 Barnard JM, Chaffin D, Droste S, Tierney A, Phernetton T. Fetal response to carbon dioxide pneumoperitoneum in the pregnant ewe. *Obstet. Gynecol.* 85(5 Pt 1), 669-74 (1995).
- 58 Barone JE, Bears S, Chen S, Tsai J, Russel JC. Outcome study of cholecystectomy during pregnancy. *Am. J. Surg.* 177, 232-236 (1999).
- 59 Hume RF, Killiam AP. Maternal physiology in obstetrics and gynecology. In: *Obstetrics and Gynecology*. Scott JR, KiSaia J, Hammon DB (Eds). JB Lippincott, PA, USA (1990).
- 60 Alexander GD, Brown EM. Physiologic alterations during pelvic laparoscopy. *Am. J. Obstet. Gynecol.* 105, 1078-1081 (1969).
- 61 Callery MP, Soper NJ. Physiology of the pneumoperitoneum. *Balliere's Clin. Gastroenterol.* 7, 757-777 (1993).
- 62 Lyass S, Pikarsky A, Eisenberg H et al. Is laparoscopic appendectomy safe in pregnant women? *Surg. Endosc.* 15, 377-379 (2001).
- 63 Affleck DG, Handrahan DL, Egger MJ, Price RR. The laparoscopic management of appendicitis and cholelithiasis during pregnancy. *Am. J. Surg.* 178(6), 523-529 (1999).
- 64 Phupong V, Suvit B. Gasless laparoscopic surgery for ovarian cyst in a second trimester patient with a ventricular septal defect. *Surg. Laparosc. Endosc. Percutan. Tech.* 17(6), 565-567 (2007).
- 65 Akira S, Yamakana A, Ishihara T, Takeshita T, Araki T. Gasless laparoscopic ovarian cystectomy during pregnancy: comparison with laparotomy. *Am. J. Obstet. Gynecol.* 3(1), 554-557 (1999).
- 66 Murakami T, Noda T, Okamura C, Terada Y, Morito Y, Okamura K. Cul-de-sac packing with a metreurynter in gasless laparoscopic cystectomy during pregnancy. *J. Am. Assoc. Gynecol. Laparosc.* 10(3), 421-423 (2003).
- 67 Schmidt T, Nawroth F, Foth D, Rein DT, Romer T, Mallmann P. Gasless laparoscopy as an option for conservative therapy of adnexal pedical torsion with twin pregnancy. *J. Am. Assoc. Gynecol. Laparosc.* 8(4), 621-622 (2001).
- 68 Romer T, Bojhar B, Schwesinger G. Treatment of a torqued hematosalpinx in the thirtieth week of pregnancy using gasless laparoscopy. *J. Am. Assoc. Gynecol. Laparosc.* 9(1), 89-92 (2002).
- 69 Oguri H, Taniguchi K, Fukaya T. Gasless laparoscopic management of ovarian cysts during pregnancy. *Int. J. Gynaecol. Obstet.* 91(3), 258-259 (2005).
- 70 Iafrati MD, Yarnell R, Schwaitzberg SD. Gasless laparoscopic cholecystectomy in pregnancy. *J. Laparoendosc. Surg.* 5(2), 127-130 (1995).
- 71 Louis-Sylvestre C, Morice P, Chapron C, Dubuisson JB. The role of laparoscopy in the diagnosis and management of heterotopic pregnancy. *Hum. Reprod.* 12, 1100-1102 (1997).
- 72 Lemaire BM, van Erp WF. Laparoscopic surgery during pregnancy. *Surg. Endosc.* 11, 15-18 (1997).
- 73 Friedman JD, Ramsey PS, Ramin KD, Berry C. Pneumoamnion and pregnancy loss after second-trimester laparoscopic Surgery. *Obstet. Gynecol.* 99(3), 512-513 (2002).
- 74 Charles R. A new technology to safely, rapidly and reproducibly pass a Veress needle. Presented at: *Society of Laparoendoscopic Surgeons 2007 Annual Meeting*. San Francisco, CA, USA, 5-8 September 2007.
- 75 Mastragelopoulos N, Sarkar MR, Kaissling G et al. Argon gas embolism in laparoscopic cholecystectomy with the Argon Beam One Coagulator. *Chirurg* 63(12), 1053-1054 (1992).
- 76 Palmer M, Miller CW, Van Way CW 3rd et al. Venous gas embolism associated with argon-enhanced coagulation of the liver. *J. Invest. Surg.* 6, 391-399 (1993).
- 77 Nezhat C, Seidman DS, Vreman HJ, Stevenson DK, Nezhat F, Nezhat C. The risk of carbon monoxide poisoning after prolonged laparoscopic surgery. *Obstet. Gynecol.* 88(5), 771-774 (1996).

Affiliations

- Linda M Nicoll, MD
Center for Special Minimally Invasive Surgery, 900 Welch Road, Suite 403, Stanford University Medical Center, Palo Alto, CA 94304, USA
Tel.: +1 650 327 8778
Fax: +1 650 327 2794
linda.m.nicoll@gmail.com
- Camran Nezhat, MD
Center for Special Minimally Invasive Surgery, 900 Welch Road, Suite 403, Stanford University Medical Center, Palo Alto, CA 94304, USA
Tel.: +1 650 327 8778
Fax: +1 650 327 2794
cnezhat@stanford.edu