2008

Nonobstetric Laparoscopy Versus Laparotomy During Pregnancy: Maternal and Fetal Outcomes

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Nonobstetric Laparoscopy Versus Laparotomy During Pregnancy:

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A Thesis Submitted to the

Yale University School of Medicine

in Partial Fulfillment of the Requirements for the

Degree of Doctor of Medicine

by

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2008

NONOBSTETRIC LAPAROSCOPY VERSUS LAPAROTOMY DURING PREGNANCY: MATERNAL AND FETAL OUTCOMES.

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The purpose of this study was to compare maternal and fetal outcomes between nonobstetric laparoscopy and laparotomy during pregnancy at Yale-New Haven Hospital. A retrospective chart review was conducted of all nonobstetric intraabdominal surgeries during pregnancy at Yale-New Haven Hospital between 1987 and 2007. Of 159 potential cases, 103 cases (57 laparoscopies, 46 laparotomies) fit the criteria for analysis. Data were collected for the maternal surgical admission, maternal delivery admission, and infant outcome for both groups, and were then analyzed using Statistical Analysis Software (SAS) Version 9.1. There was no difference in age or BMI between groups. Mean gestational age at time of surgery was higher among laparotomy patients (21.1 ± 7.9 weeks vs. 16.4 ± 7.3 weeks, $p<0.05$). There was no difference in the operative time between laparotomy and laparoscopy (79.8 ± 31.8 min vs. 86.1 ± 46.1 min, ($p=0.43$). The postoperative length of stay associated with laparotomy was double that associated with laparoscopy (4.5 ± 2.6 days vs. 2.2 ± 1.7 days, $p<0.05$). The postoperative complication rate was 47.4% after laparotomy and 17.4% after laparoscopy ($p<0.05$). There were no maternal deaths. Three fetal losses occurred but did not reach statistical significance. Mean gestational age at delivery, Apgar scores, and rate of low-birth-weight infants were comparable between groups. Our data demonstrate that nonobstetric laparoscopy during pregnancy maintains the advantages of minimally invasive surgery and has better maternal and fetal outcomes than nonobstetric laparotomy during pregnancy.

Acknowledgements

I would like the thank the following people for their assistance, without whom completing this thesis would have been impossible: Dr. Kurt Roberts, YSM Department of Surgery, Dr. Jason Prescott, YNHH Resident in General Surgery, Dr. John Geibel, YSM Department of Surgery, Dr. John Forrest, YSM Office of Student Research, Dr. Valentine Njike, Yale Prevention Research Center, Dr. James Barone, Lincoln Medical Center Department of Surgery, Mae Geter, YSM Office of Student Research, Donna Carranzo, YSM Office of Student Research, Jan Glover, YSM personal librarian, Sue Roberts, YNHH Medical Records, Karen East, YNHH Certified Coding Specialist, Marina Kashtelyan, YNHH IT&T System Analyst II, Cheryl Raab, YNHH Perinatal Patient Safety Nurse, Sandra Ryan, YNHH Vital Statistics Chief Clerk, and Federico Amadeo, Connecticut Department of Public Health. Special thanks to Jacob William Ruby, Gay Alberts Ruby, John Jacob Ruby, Heather Michelle McGee, Christina Whitney Schmidt, and Kara Veleta Mulrooney.

This project was supported financially by the Yale School of Medicine Office of Student Research Short-Term Research Stipend.

HIC Protocol # 0710003204.

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Introduction

Surgery in Pregnancy

Surgical intervention during pregnancy strives to alleviate maternal disease while concurrently minimizing fetal harm. Acute surgical disease in and of itself increases maternal and fetal morbidity and mortality; the severity of the underlying surgical disease, as opposed to the surgery itself, may be the strongest factor influencing maternal and fetal outcome [1]. When a gravid patient presents with an acute abdomen, the risks and benefits to both the mother and fetus must be weighed for each step of the work-up and treatment plan. When an emergent operation is indicated, the surgery should not be withheld on the sole basis of the patient's gravid state [1, 2]. On the contrary, the alleviation of maternal disease is thought to take priority, in general, because the health of the fetus depends on the health of the mother [3]. The risks of surgery during pregnancy have been reduced by improvements in both maternal perioperative care and neonatal intensive care, nevertheless, "any surgery during pregnancy is not an innocent procedure, and caution should always be exercised" [4, 5].

Abdominal pain during pregnancy may result from a myriad of pathologies, including common general surgical problems such as appendicitis, acute cholecystitis, and small bowel obstruction; obstetric problems such as ectopic pregnancy, miscarriage, and placental abruption; and normal physiologic changes, such as stretching of the round ligaments [6]. While early diagnosis and treatment usually translates into improved maternal and fetal outcomes, reaching the correct diagnosis can be a challenge due to the confounding physiologic changes of pregnancy. The abdominal wall muscles grow more lax during late pregnancy, making the absence of peritoneal signs a less conclusive physical finding [7, 8]. The enlarging uterus may also alter normal anatomical landmarks; for example, the appendix may be displaced out of the right lower quadrant into the right lateral upper quadrant, which can make appendicitis more difficult to diagnose [9]. Leukocystosis, usually considered an important laboratory finding, is less useful among pregnant patients because the leukocyte count during normal pregnancy ranges from 5,000 to 12,000/µL and elevates to an average of 14,000 to 16,000/µL during labor [10]. The symptoms of nausea and vomiting may also be misleading, as nearly 50% of women experience nausea and vomiting during pregnancy [3].

The incidence of nonobstetric surgery during pregnancy has been variably reported as one in 133 to one in 833 [11, 12]. The category of intraabdominal surgery composes the largest portion of these surgeries, making up 24.6%, of all nonobstetric surgeries during pregnancy [12]. Since procedures that can be considered elective are generally postponed until the patient is postpartum, the most common surgeries performed during pregnancy arise from the acute illnesses of appendicitis, cholecystitis, and intestinal obstruction [2, 13].

Intraabdominal surgery during the first trimester has historically been associated with increased risk of spontaneous abortion and teratogenesis, therefore some surgeons concluded that surgery is contraindicated during the first trimester [14]. The rate of miscarriage after first trimester nonobstetric surgery was found to be 10.5% in a literature review by Cohen-Kerem *et al* [11]; however, the significance of this rate cannot be determined in the absence of a control group. Teratogenesis is perceived as a risk because organogenesis occurs during the first trimester; the heart, for example, begins developing around four weeks gestation and begins pumping blood from all four chambers by six weeks gestation [15]. Cohen-Kerem[11] noted a 3.9% rate of major birth defects among patients operated on during the first trimester, compared to a 2.0% rate among all gravid surgical patients. These values are close to the expected major birth defect rate in the total population, estimated at 1-3% [11].

Just as surgery during the first trimester is avoided due to an increased risk of spontaneous abortion and teratogenesis, surgery during the third trimester is warned against due to an increased risk of preterm delivery [16]. Kort *et al* [2] described a 25.7% rate of preterm delivery within two weeks of nonobstetric surgery performed in the third trimester, triple the 8.2% rate seen in the second trimester (p<0.05). Therefore, the second trimester was deemed the ideal time for intraabdominal surgical intervention, as it minimized the risks of spontaneous abortion, teratogenesis, and preterm delivery.

Laparoscopy in Pregnancy

Laparoscopic techniques have been used during pregnancy by obstetricians and gynecologists since the 1970's, primarily to diagnose and treat ectopic and heterotopic pregnancies [17]. Within the field of general surgery, however, pregnancy was considered an absolute contraindication to laparoscopy as recently as 1991 [18].

Laparoscopic cases performed in pregnant patients range from appendectomy, cholecystectomy, bowel resection, and lysis of adhesions, to the uncommon adrenalectomy, splenectomy, transperitoneal nephrectomy, lymphadenectomy, symptomatic hernia repair, and liver biopsy [13, 19-21]. As laparoscopic technology advances, and surgeon's laparoscopic skills improve, the number and variety of laparoscopic cases performed in pregnant patients is expected to increase [22].

Diagnostic laparoscopy has been proposed as one possible solution to the diagnostic quandary of acute abdominal pain of unknown etiology. Diagnostic laparoscopy is touted as a safe and effective tool to simultaneously diagnose and surgically treat acute abdominal processes [13]. Laparoscopy allows for a thorough abdominal exploration by providing a magnified and panoramic view of the intraabdominal contents [23]. The ability to explore the abdomen laparoscopically, with minimal uterine manipulation, is postulated to decrease uterine irritability and consequently decrease the risk of postoperative contractions, spontaneous abortion, and premature delivery [16].

Curet *et al* [16] performed a six-year case-control study from 1990 through 1995, comparing 16 laparoscopies to 18 laparotomies during pregnancy. The laparoscopic group had significantly longer operative times, but had the advantages of shorter hospitalization, earlier resumption of regular diet, and decreased duration of narcotic use. The increased operative time was attributed to the initial learning curve for laparoscopy, suggesting that operative times are likely to decrease as laparoscopic skill levels increase. In addition, these longer operative times may be partially accounted for by the differences in procedures between the laparoscopic and control group, as there were three more appendectomies and one less cholecystectomy performed in the open group. Three maternal complications were noted: a trocar fascial hernia diagnosed one-year postoperatively, preterm labor, and pregnancy-induced hypertension. The incidence of fetal complications observed was within the range seen in non-surgical pregnancies at the same institution [16]. The authors concluded that no significant differences existed in the maternal and fetal morbidity and mortality between laparoscopic and open patients.

The largest series of laparoscopic surgery during pregnancy in the 1990's was published by Affleck *et al* [24], who compared 19 laparoscopic appendectomies and 42 laparoscopic cholecystectomies to open controls. The authors found no statistically significant difference in preterm delivery rates, birth weights, or Apgar scores between the open and laparoscopic approach. At their institution, laparoscopy is offered to gravid patients as a first-line approach [24].

In 2002, Oelsner *et al* [25] published a multicenter retrospective study comparing 192 laparoscopies with 197 laparotomies during pregnancy, and found no differences in rates of spontaneous abortion, preterm delivery, intrauterine growth restriction, or fetal anomalies. In addition, there was no difference in the mean operating time, and the laparoscopic patients had fewer complications and shorter hospitalizations [25].

Eight years after Mazze and Källén [12] published their analysis of surgery during pregnancy based on the Swedish health registries, Reedy *et al* [26] used the Swedish health registries to compare the fetal outcome of 2181 laparoscopies and 1522 laparotomies in patients with singleton pregnancies between four and 20 weeks gestational age. They found no differences between the two groups in gestational age at delivery or in rates of low-birth-weight infants, congenital anomalies, or cumulative infant death, although spontaneous abortions were not examined [26].

Reedy *et al* [22]surveyed the Society of Laparoendoscopic Surgeons on the topic of laparoscopy during pregnancy in 1997; 192 laparoscopic surgeons returned surveys, describing a total of 413 laparoscopic cases, including 199 cholecystectomies and 67 appendectomies. The survey focused on intraoperative and postoperative laparoscopic complications; demonstrating a 4% incidence of spontaneous abortion after first-trimester laparoscopy, an incidence comparable to that within the total population. The authors concluded that the safety of laparoscopy during pregnancy is similar to laparotomy during pregnancy. The strength of the Reedy study is limited by recall bias (the data were collected retrospectively) and by selection bias (surgeons who responded to the survey may have been those who had good outcomes). In addition, the survey was only distributed to SLS members, a group of surgeons who may have more advanced laparoscopic skills than non-member surgeons [22].

There exists one long-term follow-up study of childhood outcomes after laparoscopic surgery in pregnancy; Dr. Anne Rizzo [27] monitored eleven children whose mothers had undergone laparoscopic cholecystectomy (n=5), appendectomy (n=4), or lysis of adhesions (n=2) up to eight years postoperatively and found no developmental abnormalities, physical abnormalities, or major medical problems among any of the children [27].

Numerous case reports and case series have concluded that laparoscopy has no greater maternal and fetal morbidity and mortality than laparotomy during pregnancy [28-36]. If clinical outcomes are indeed equivalent, then laparoscopy could be seen as preferable to laparotomy if the proven benefits of laparoscopic surgery among the general public hold true for pregnant patients [17].

Laparoscopy during pregnancy has been shown to decrease hospital stay and to allow for an earlier return to normal activity [16]. The bowel manipulation necessary during laparoscopy may be less than that of laparotomy, and thus laparoscopy is thought to cause fewer postoperative adhesions and to decrease the incidence of intestinal obstruction [5, 37]. In addition, the faster return of gastrointestinal tract function seen in laparoscopy results in an earlier return to enteral nutrition, which may decrease fetal nutritional stress [38]. The finding of earlier ambulation after laparoscopy decreases the risk of deep vein thrombosis and subsequent embolic events, touted as the leading cause of maternal mortality in the United States [39, 40]. Laparoscopy's smaller incisions not only offer improved cosmesis but also decrease the incidence of incisional hernias, wound infections, and wound dehiscence [38]. Pregnant patients are especially at risk for herniation due to increased abdominal wall tension during pregnancy [39]. Smaller incisions are considered less painful and therefore decrease maternal narcotic demand [41]. Decreasing maternal narcotic use is beneficial to the fetus, as narcotic use is associated with fetal depression, as well as maternal pulmonary depression, which can cause maternal hypoventilation, atelectasis, and eventually, fetal acidosis [38].

The introduction of laparoscopic techniques added a twist to the equation of planning surgery during pregnancy. Laparoscopy is the least technically difficult during the first trimester, when the uterus remains below the level of the pubic symphysis [10, 42]. The technical difficulty increases with gestational age, as the enlarging uterus increasingly interferes with the instrumentation and visualization of the operative field necessary to safely complete laparoscopic procedures [14, 43]. Initially, a gestational age of 28 weeks was proposed as the upper limit for laparoscopy, in part due to reports of third-trimester laparoscopy requiring conversion to laparotomy due to poor exposure [5, 16]. Despite these warnings, laparoscopic appendectomies and cholecystectomies have both been performed in patients with pregnancies at 34 weeks gestation [44, 45]. There are many who now believe that laparoscopy can be performed safely during any trimester of pregnancy [13].

In October 2000, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) [46] published a revision of their 1998 guidelines for laparoscopic surgery during pregnancy. The document gave eight specific recommendations on techniques for performing laparoscopy during pregnancy, however, citing a lack of long-term clinical studies, it neither encouraged nor discouraged the use of the laparoscopic approach [46]. In September 2007, SAGES [13] revised its guidelines again to incorporate recent data supporting the use of laparoscopy during pregnancy. As in its previous version, the document neither encourages nor discourages the use of laparoscopy for appendectomies or solid organ resections during pregnancy. However, laparoscopy is recommended over laparotomy in one situation: cholecystectomy. Guideline 15 states, “laparoscopic cholecystectomy is the treatment of choice in the pregnant patient with gallbladder disease regardless of trimester” [13].

Appendectomy

Appendicitis during pregnancy has been shown to have an incidence of approximately one in 766 pregnancies to one in 3000 pregnancies, making appendectomy the most common nonobstetric surgery performed during pregnancy [24, 47]. Appendicitis is equally likely to occur during any of the three trimesters [39]. One hundred years ago, Babler [48] cautioned, “the mortality of appendicitis complicating pregnancy is the mortality of delay.” Indeed, the perforation rate of pathologically-confirmed acute appendicitis ranges from 13 to 60% among pregnant patients in general, and perforated appendicitis is the most common surgical cause of fetal loss [2, 24]. Maternal mortality may be as high as 4% in pregnant patients with perforated appendicitis and generalized peritonitis, although McGory *et al* [47] noted that maternal mortality from appendicitis during pregnancy was trending downward over the years, "from 40% in 1908, to 0.9% in 1976, to virtually zero in our study" [3]. Fetal loss is reported to range from 1.5-2.6% in pregnant patients with uncomplicated appendicitis, to 10.9-20% in cases of perforated appendicitis, to 35.7% in cases of generalized peritonitis [1, 9, 11].

The largest study of appendectomy during pregnancy is a retrospective analysis of the California Inpatient File by McGory *et al* [47], which found a 4% rate of fetal loss and 7% rate of preterm delivery among 3,133 laparoscopic and open appendectomies performed during pregnancy. The authors state that their data may underestimate the rates of fetal loss and early delivery because fetal loss and preterm delivery were only counted if they occurred during the same inpatient hospitalization as the appendectomy. In addition, the preterm delivery rate may be underestimated because the preterm delivery rate was based solely on the procedure codes for cesarean section or hysterectomy, and thus does not include preterm vaginal deliveries [47].

Regardless of the exact rate of fetal loss, appendicitis and the standard of care treatment of appendectomy have been shown to negatively effect fetal outcome. A review of Swedish health care registries by Mazze and Källén [49] focused on 778 cases of open appendectomy during pregnancy and found an increased risk of preterm delivery in third trimester surgeries, a decrease in the average birth weight, and an increased incidence of perinatal death as compared to the values from the total population of Sweden.

The rate of false-positive appendicitis during pregnancy is approximately 23% to 50%, a range significantly higher than the 20% rate of false-positive appendicitis reported in nonpregnant women [43, 50]. A recent retrospective chart review of appendectomy during pregnancy found a 54% rate of false-positive appendicitis based on clinical evaluation alone, 36% with ultrasound evaluation alone, and 8% with the combination of ultrasound and computed tomography (CT) scan [51]. Since the morbidity and mortality of appendicitis during pregnancy is thought to result in part from a delay in diagnosis, immediate surgery is recommended once appendicitis has been diagnosed [3]. Even without a definitive diagnosis, the clinical suspicion of appendicitis during pregnancy can be cause for immediate surgical exploration, as the prevention of appendiceal perforation and its associated risk of fetal loss outweighs the consequence of an increased rate of false-positive appendicitis [43].

Laparoscopic appendectomy has been suggested to be the procedure of choice in all stages of pregnancy [39]. In 2002, a retrospective study by Rojasnky *et al* [52] noted a trend toward reduced rates of premature labor and a statistically significant lower rate of intrauterine growth restriction in pregnant patients undergoing laparoscopy (primarily laparoscopic appendectomy), as compared with laparotomy. Three years later, however, Carver *et al* [53] compared maternal and fetal outcomes after open and laparoscopic appendectomy in the first two trimesters and found no statistically significant difference in length of hospitalization, wound infection rate, complication rate, or birth weight. Two spontaneous abortions were reported among the laparoscopic appendectomy patients versus no spontaneous abortions in the open appendectomy patients; though not statistically significant, the authors suggest that the fetal losses had clinical significance and concluded that laparoscopy did not demonstrate any advantages over laparotomy [53]. Finally, McGory *et al* [47] noted a 7% fetal loss rate in laparoscopic appendectomy, which more than doubled the 3% fetal loss rate observed in open appendectomy, leading the authors to conclude that laparoscopic appendectomy imposed a greater risk to the fetus.

Taken together, the above presented data support a proactive approach to the work-up and management of suspected appendicitis. While maternal and fetal outcomes associated with appendicitis have improved over time, appendicitis, and perforated appendicitis in particular, increases maternal and morbidity and mortality. No consensus exists among general surgeons as to the preferred surgical approach for performing appendectomies during pregnancy.

Cholecystectomy

Cholecystectomy is the second most common general surgical procedure performed during pregnancy (behind appendectomy). Pregnancy is associated with an increased risk for developing and retaining gallstones [54]. During pregnancy, gallbladder contractility decreases and its residual volume doubles in size; this decreases gallbladder emptying and increases bile stasis [10, 45]. In addition, hormonal changes during pregnancy increase the saturation of bile with cholesterol, which contributes to the formation of cholesterol crystals and, eventually, cholesterol stones [10].

Symptomatic cholelithiasis affects five to ten out of every 10,000 pregnancies, and the cholecystectomy incidence is around half that value, occurring in one to six out of every 10,000 pregnancies [4, 24, 55]. Patients with symptomatic cholelithiasis during pregnancy are usually initially managed medically, with intravenous hydration, oral intake restriction, analgesics, and antibiotics, in an attempt to defer surgery until after delivery [14]. While the majority of pregnant patients with symptomatic cholelithiasis can be managed medically until postpartum, up to 41% will require cholecystectomy during pregnancy [4, 56]. Surgical intervention is generally indicated for associated conditions such as gallstone pancreatitis, peritonitis, obstructive jaundice, multiple hospitalizations, acute cholecystitis refractory to medical management, nausea and vomiting causing maternal weight loss or a lack of maternal weight gain, and intrauterine growth restriction [24, 57, 58].

Historically, patients requiring cholecystectomy were managed medically during the first trimester and then scheduled for an elective cholecystectomy during the second trimester [56]. The disadvantage of forcing patients to wait until the second trimester for a cholecystectomy is best put into words by Dixon *et al* [56], who wrote, “abortion was induced in three patients during the first trimester because of persistent or recurrent symptoms and the desire for early cholecystectomy.”

The second trimester is considered the optimal time for elective cholecystectomy. McKellar *et al* [4] described a 12.0% rate of spontaneous abortion after first-trimester open cholecystectomy, more than double the 5.6% rate of spontaneous abortion observed after second-trimester open cholecystectomy. McKellar *et al* also found that postoperative contractions occurred after 40% of third-trimester open cholecystectomies, compared to 0% after second-trimester open cholecystectomy. Despite the occurrence of postoperative contractions after third-trimester open cholecystectomies, there were no documented premature deliveries; therefore the clinical significance of the contractions is debatable [4].

The first laparoscopic cholecystectomies performed during pregnancy were described in three case reports published in 1991 [38, 59, 60]. The case report by Pucci and Seed [38] is remarkable in that the surgery was performed at 31 weeks gestational age, weeks beyond what some surgeons deemed the limit of laparoscopy during pregnancy. The patient went on to deliver a full-term healthy infant, and the authors concluded, "We believe pregnancy is not a contraindication to a laparoscopic cholecystectomy, and the procedure provides marked benefits for the patient who needs removal of the gallbladder during pregnancy" [38]. Barone *et al* [37] reviewed 20 laparoscopic cholecystectomies during pregnancy and 26 open cholecystectomies during pregnancy throughout the state of Connecticut, and found decreased rates of postoperative contractions and fetal distress among the laparoscopic patients.

In a literature review of 68 laparoscopic cholecystectomies by Graham *et al* [61], none of the first-trimester patients followed to delivery underwent spontaneous abortion, and 21% of third-trimester patients experienced postoperative contractions. As these rates are less than the 12% rate of spontaneous abortion and 40% rate of postoperative contractions reported after open cholecystectomy, the authors concluded that the laparoscopic approach was safer for first- and third-trimester cholecystectomies [4, 61].

Cholecystectomy is currently the most common laparoscopic procedure performed during pregnancy [22]. With advancements in laparoscopic technique, the approach most commonly utilized for cholecystectomy during pregnancy has shifted from open to laparoscopic cholecystectomy. Laparoscopic cholecystectomy is now the standard of care for cholecystectomy during pregnancy in at least one institution [62]. Likewise, there is a trend toward surgical management instead of medical management for symptomatic cholelithiasis; at UCSF, 47% of pregnant patients with symptomatic cholelithiasis are treated surgically, as compared to 13% prior to 1990 [17].

Complications of Surgery in Pregnancy

Maternal death has been reported following nonobstetric surgery during pregnancy, after both laparotomies and laparoscopies. Barone *et al* [37] published the case of a 27 year old woman who underwent elective laparoscopic cholecystectomy at 20 weeks gestational age and died of intraabdominal hemorrhage two weeks postoperatively. Allen *et al* [63] looked at laparotomy during pregnancy, and reported two maternal-fetal deaths among 90 patients. The first maternal-fetal death was in a patient with cryptogenic cirrhosis who underwent an operation for mesenteric venous occlusion and small bowel infarction, the second maternal-fetal death was in a patient with inflammatory bowel disease who underwent three operations for ischemia and ileostomy obstruction and then experienced cardiopulmonary arrest [63].

Complications examined among pregnant patients who have undergone laparoscopy include enterotomy, severe abdominal pain caused by carbon dioxide (CO_2) pneumoperitoneum, and uterine perforation [22]. Dr. Kerrey Buser [64] described one uterine perforation that occurred during laparoscopic surgery via manipulation of a blunt 10-mm port canula; no uterine repair was deemed necessary and the patient delivered “later in the pregnancy” by cesarean section (exact gestational age is not given). In contrast to this seemingly benign outcome of a uterine perforation, dire consequences have been documented. Friedman *et al* [65] reported the case of a patient at 21 weeks gestation who underwent diagnostic laparoscopy and appendectomy; subsequent abdominal CT demonstrated a pneumoammnion, attributed to direct uterine trauma and carbon dioxide insufflation, and the patient delivered a stillborn shortly thereafter.

The most well-known case series reporting poor fetal outcomes after laparoscopy, written by Amos *et al* [66], describes four fetal deaths among seven patients who underwent laparoscopic surgery during pregnancy. Three of the four fetal deaths occurred in patients treated surgically for gallstone pancreatitis and ruptured appendicitis, conditions known to have adverse fetal outcomes. The authors posit that the fetal deaths were due to the inflammatory process rather than the surgical procedure. This sentiment is echoed by de Perrot *et al* [43], who attributed the fetal deaths “to underlying maternal disease… to a tendency to have more advanced disease, and to the underlying disease processes rather than to the laparoscopic procedure.” Still, Amos *et al* [66] hedge their bets by concluding, “we have currently abandoned laparoscopic surgery during pregnancy.”

Research Aims

The purpose of this retrospective case series is to determine whether our experiences at Yale-New Haven Hospital (YNHH) support laparoscopy as the standard of care for intraabdominal nonobstetric surgery during pregnancy. We aim to:

1. Determine if laparoscopic surgery during pregnancy confers the same surgical advantages of laparoscopic surgery versus open surgery as seen in the general population, such as decreased postoperative length of stay and decreased incidence of wound infection, without increased operative time.
2. Evaluate maternal and fetal outcomes for singleton pregnancies complicated by:

    a.) Laparoscopy and laparotomy, across all categories

    b.) Laparoscopic and open appendectomy

    c.) Laparoscopic and open cholecystectomy

    The specific outcome parameters to be evaluated include the incidence of spontaneous abortion, stillbirth, perinatal death, congenital anomalies, and breathing difficulties, as well as the average gestational age at delivery, birth weight, and Apgar scores.

Hypothesis

Nonobstetric laparoscopy during pregnancy at YNHH maintains the well-described advantages of laparoscopic surgery in general and has an incidence of maternal and fetal morbidity and mortality that is equal to that of nonobstetric laparotomy during pregnancy at YNHH.

Methods

Literature Search

A review of the current literature was conducted under the guidance of Jan Glover, a Yale School of Medicine education services librarian. The Medline database was searched using the Medical Subject Headings (MeSH) terms (pregnancy complications/surgery and (laparotomy or laparoscopy)) and (pregnancy outcomes or birth weight or gestational age or fetal death or fetal growth retardation). Studies were included if they were published in English and consisted of human subjects. Literature published prior to 1985 was excluded from the initial review because of the paucity of general surgery laparoscopy cases published prior to 1985. Subsequently, pertinent references from the retrieved articles led to the inclusion of a handful of articles published prior to 1985 and/or containing animal subjects.

Chart Review

Patients were selected for the chart review using diagnosis and procedure codes from the International Classification of Diseases, 9th Revision (ICD-9), with the assistance of Karen East, a YNHH Certified Coding Specialist. The ICD-9 codes used to identify patients included diagnosis codes 640-677 with the fifth digit being one, two, or three (complications related to pregnancy, indications for care in pregnancy, and complications occurring in the course of labor and delivery), and procedure codes 07.2x, 07.3x, 07.4x, 41.4x, 41.5x, 45.xx, 46.xx, 47.xx,48.xx, 50.xx, 51.0x, 51.2x, 51.3x, 51.4x, 51.7x, 51.9x, 52.xx, 53.xx, and 54.xx (operations on endocrine glands, the spleen, and the digestive system). After the diagnostic and procedure codes were identified, a list of prospective patients was generated by Marina Kashtelyan, a YNHH IT&T System Analyst. The initial list included 487 female patients who underwent laparotomy or laparoscopy during pregnancy from 1987 to 2007. This list of 486 patients was edited to 159 patients by analyzing the procedure codes and excluding patients who underwent a primarily obstetric surgery. Examples of patients excluded include those who underwent diagnostic laparoscopy to rule out ectopic pregnancy, and those who underwent a cesarean section with concurrent lysis of adhesions. Charts were then requested from medical records for the remaining 159 patients. All charts were obtained through the YNHH medical records department, as coordinated by medical records employee Sue Roberts. Of these 159 requested charts, 158 charts were available for review, of which 133 were selected as appropriate for this study. The reasons for the exclusion of 25 of the 158 initial cases included primarily obstetric or gynecologic surgery [ovarian cystectomy (1), rule out ectopic pregnancy (4), abdominal cerclage (1)], medically managed condition (1), surgery that did not fit our criteria for intraabdominal surgery [open umbilical hernia repair (3), open inguinal hernia repair (2), cholecystostomy (1)], and postpartum state at time of surgery (12).

Data Collection

The following maternal data were collected for the primary, surgical admission: year, age, race, gravidy, parity, gestational age, singleton vs. twin, total length of stay, postoperative day at discharge, height, weight, BMI, type of operation, operative time, intraoperative complications, postoperative complications, surgical findings, pathologic findings, usage of fetal heart monitoring, tocolytics given, and presence of contractions. When available, the number of readmissions between the time of the surgery and the time of delivery was recorded. To evaluate obstetric outcome, the following maternal data were collected: fetal loss through spontaneous abortion, fetal loss through therapeutic abortion, fetal loss through stillbirth, delivery through vaginal delivery, indication for induction of labor (if induced), delivery through cesarean section, indication for cesarean section, and location of delivery (Yale-New Haven Hospital vs outside hospital). To analyze fetal outcome, the following fetal data were collected: gestational age at delivery, postoperative week at delivery, sex, birth weight, Apgar score at one and five minutes, presence of congenital anomaly, respiratory function, length of hospital stay, and occurrence of perinatal death.

Birth statistics for YNHH at large were obtained with the help of Cheryl Raab, YNHH Perinatal Patient Safety Nurse, Sandra Ryan, YNHH Vital Statistics Chief Clerk, and Federico Amadeo, Connecticut Department of Public Health.

Data Analysis

Data were analyzed with the assistance of Dr. Valentine Njike, of the Yale Prevention Research Center. Statistical Analysis Software (SAS) Version 9.1 was used for calculations of the mean, confidence interval, standard deviation, standard error of the mean, and the *p*-value using the Welch-Satterthwaite t test, pooled-variance t test, Fisher's exact test, and chi-square test, as appropriate. A p-value < 0.05 was considered statistically significant.

Results

Definitions

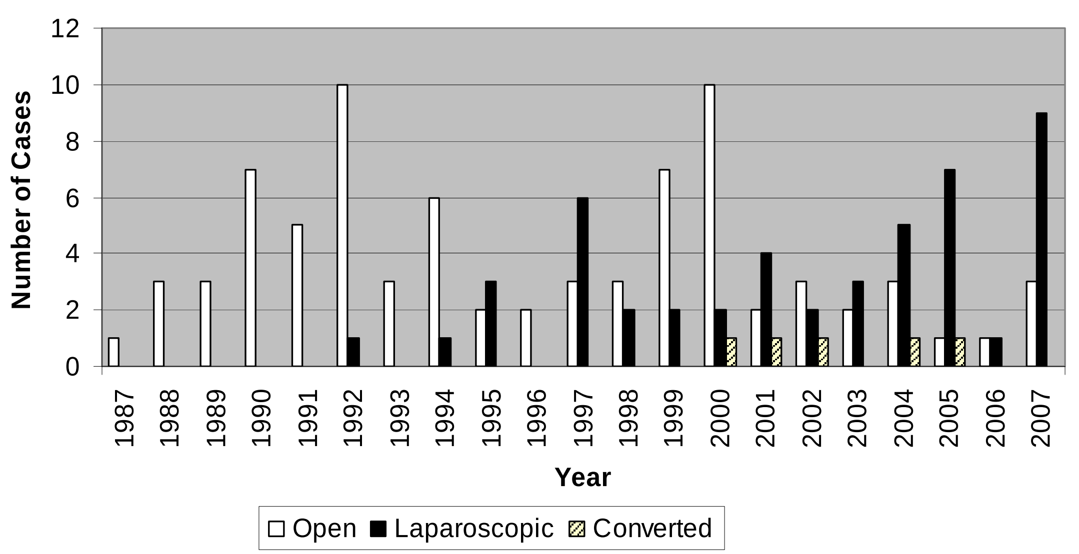
For the purposes of our analysis, first trimester is defined as 1-12 weeks, second trimester as 13-24 weeks, and third trimester as 25 weeks and beyond. For clarification, a patient at a gestational age of 12 weeks and six days was counted as being in the first trimester; likewise, a patient at 24 weeks and six days was counted as being in the second trimester. We define low birth weight as less than 2500g, and very low birth weight at less than 1500g. Spontaneous abortion, commonly referred to as miscarriage, refers to a pregnancy that ends when the fetus weighs 500g or less and/or before the fetus has reached 20 weeks gestation. Any deliveries after 20 weeks would be recorded as a stillbirth, preterm delivery, or full term delivery. We define stillbirth as death of the fetus weighing greater than 500g and/or with a gestational age of greater than 20 weeks prior to extraction from the mother. We define preterm delivery as delivery before 37 weeks gestation. We define perinatal death as fetal death occurring within seven days of birth.

We define a complication as any event of potentially harmful clinical significance that may be attributed to surgery. Spontaneous abortions and preterm deliveries are counted as postoperative complications if the delivery occurred within seven days of the surgery, or if the delivery occurred during the same hospitalization as the surgery. Therefore, not every spontaneous abortion and preterm delivery is counted as a complication. Postoperative contractions are only counted as a complication in the absence of preoperative contractions. We do not use the phrase “preterm labor” to describe postoperative contractions because the word “labor” implies that the uterine contractions have produced cervical change. In order to accurately represent the incidence of postoperative contractions that do not lead to preterm delivery, postoperative contractions are only considered a complication if the patient does not have the complication of preterm delivery. The conversion from spinal to general anesthesia is not considered a complication, as we deem this to be an appropriate action for ensuring patient safety.

Frequency of Surgery During Pregnancy at YNHH

One hundred and thirty-three cases of nonobstetric intraabdominal surgery during pregnancy took place at YNHH between the years of 1987 and 2007, with an incidence ranging from one to 13 cases per year (Figure 1). A total of 85,988 infants were delivered at our institution in the years for which annual data are available, 1990 to 2007. During that same period of time, 126 nonobstetric intraabdominal surgeries were performed, including 74 appendectomies and 35 cholecystectomies; the incidence of nonobstetric intraabdominal surgery was one in 682 deliveries, and for appendectomy and cholecystectomy, one in 1,162 and one in 2,457 deliveries, respectively.

Figure 1. Operative Approach by Year



Laparotomy vs. Laparascopy

The first nonobstetric laparoscopic surgery performed during pregnancy at YNHH occurred in 1992 (Figure 1). For better comparison, the 19 nonobstetric laparotomies performed before 1992 were excluded, leaving 114 cases for potential analysis. Of these 114 cases, six were excluded because they were performed on patients with twin gestations. These six cases were thrown out because, even within the healthy population, twin pregnancy outcomes differ greatly from singleton outcomes. Additionally, five conversion (laparoscopic-to-open) cases were excluded to avoid confounding the results of the laparotomy group with patients who underwent pneumoperitoneum prior to the conversion to laparotomy. Therefore, this study analyzes the outcomes of 103 cases (57 laparotomies, 46 laparoscopies) of nonobstetric intraabdominal surgery during pregnancy at YNHH between 1992 and 2007.

The racial backgrounds of the patients included 42 White non-Hispanics, 35 Hispanics, 22 Blacks, and 4 Asian/Pacific Islanders. There were no maternal deaths. The patients who underwent laparotomic and laparoscopic surgeries were comparable in age and body mass index (BMI) (Table 1). The gestational age at the time of surgery was higher for open (mean=21.1 ± 7.9 weeks, n=57) than laparoscopic (mean=16.4 ± 7.3 weeks, n=46) surgery ($p<0.05$, pooled-variance t test). While there was a trend towards decreased operative time in the open group, there was no statistical difference between open (79.8 ± 31.8 min, n=57) and laparoscopic (86.1 ± 46.1 min, n=46) operative time ($p=0.43$, Welch-Satterthwaite t test, Table 1).

Fetal heart rate monitoring was utilized preoperatively in 74% (76/103) of all cases and postoperatively in 80% (82/103) of all cases; in contrast, postoperative fetal heart monitoring was used in just 18% (19/103) of cases. Five percent of patients (n=5) had both pre- and postoperative contractions. Of the patients who did not have preoperative contractions, 19.3% (n=11) of patients who had open surgery and 2.2% (n=1) of patients who had laparoscopic surgery experienced postoperative contractions ($p<0.05$, chi-square test, Table 1). Of the ten patients given prophylactic tocolytics postoperatively, 10% (n=1) experienced postoperative contractions; this is similar to the 12.5% (n=11) of patients who did not receive prophylactic tocolytics and who experienced postoperative contractions.

The total length of stay was longer for the open (5.5 ± 3.1 days, n=57) patients than for the laparoscopic (3.7 ± 3.8 days, n=46) patients ($p<0.05$, pooled-variance t test), and the postoperative length of stay for open (4.5 ± 2.6 days, n=57) patients was doubled that of the laparoscopic (2.2 ± 1.7 days, n=46) patients ($p<0.05$, Welch-Satterthwaite t test, Table 1). The rate of postoperative complications was significantly higher after open surgery, with postoperative complications reported in 47.4% (n=27) of open patients and just 17.4% (n=8) of laparoscopic patients ($p<0.05$, chi-square test, Table 1).

Of the 103 patients, delivery information was available for 79% of patients (n=81). There was one spontaneous abortion, one therapeutic abortion, one stillbirth, and there were 78 live-born infants. Fetal losses due to spontaneous abortion and stillbirth are described within the appendectomy subgroup results. There were no documented accounts of perinatal death. The rate of vaginal delivery was 79.5% (n=35) after open surgery and 58.8% (n=20) after laparoscopic surgery ($p=0.14$, chi-square test, Table 1). These data are not statistically significant, therefore there is no increased risk of cesarean section following open surgery versus laparoscopic surgery during pregnancy. There was no difference in the gestational age at the time of delivery, however, due to the open surgeries being performed at a later gestational age, the length of time between surgery and delivery was shorter for open (15.3 ± 9.2 weeks, n=46) than laparoscopic (21.8 ± 7.6 weeks, n=34) procedures (p<0.05, pooled-variance t test, Table 1).

The average birth weight was lower among infants whose mothers underwent open (2902 ± 734 grams, n=37) surgery, as compared to laparoscopic (3324 ± 664 grams, n=30) surgery (p<0.05, pooled-variance t test). There were no differences between Apgar scores at one and five minutes, preterm delivery rate, and the low-birth-weight rate between the open and laparoscopic approaches (Table 1).

	Open			Laparoscopic				
	Mean	**n**	**S.D.**	**Mean**	**n**	**S.D.**	***p*- value**	**Method**
Maternal Age	27.0 years	57	7.2	26.0 years	46	5.8	NS[A]	Pooled-variance t test
Body Mass Index (BMI)	28.0	53	5.5	30.3	45	8.9	NS	Welch-Satterthwaite t test
Gestational Age at Surgery	21.1 weeks	57	7.9	16.4 weeks	46	7.3	<0.05	Pooled-variance t test
Operative Time	79.7 min	57	31.8	86.1 min	46	46.1	NS	Welch-Satterthwaite t test
Total Length of Stay	5.5 days	57	3.1	3.7 days	46	3.8	<0.05	Pooled-variance t test
Post-Operative Length of Stay	4.5 days	57	2.6	2.2 days	46	1.7	<0.05	Welch-Satterthwaite t test
Gestational Age at Delivery	37.3 weeks	46	5.0	38.5 weeks	34	2.4	NS	Welch-Satterthwaite t test
Time Between Surgery and Delivery	15.3 weeks	46	9.2	21.8 weeks	34	7.6	<0.05	Pooled-variance t test
Birth Weight	2902 grams	37	734	3324 grams	30	664	<0.05	Pooled-variance t test
1 min Apgar	7.8	43	2.3	8.3	32	1.6	NS	Welch-Satterthwaite t test
5 min Apgar	8.3	43	1.7	8.8	32	0.9	NS	Welch-Satterthwaite t test
Intraoperative Complication	5.3%	3/57		2.2%	1/46		NS	Fisher's exact test
Postoperative Complication	47.4%	27/57		17.4%	8/46		<0.05	Chi-square test
Postoperative Contractions	19.3%	11/57		2.2%	1/46		<0.05	Chi-square test
Vaginal Delivery	79.5%	35/44		58.8%	20/34		NS	Chi-square test
Preterm Delivery	20.0%	9/45		11.8%	4/34		NS	Chi-square test
Low Birth Weight	16.2%	6/37		3.3%	1/30		NS	Fisher's exact test

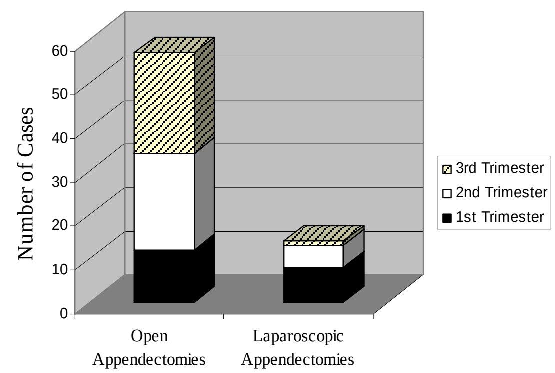
Table 1. Comparison of open and laparoscopic surgeries during pregnancy by maternal and fetal parameters
[A] Not statistically significant

Appendectomies

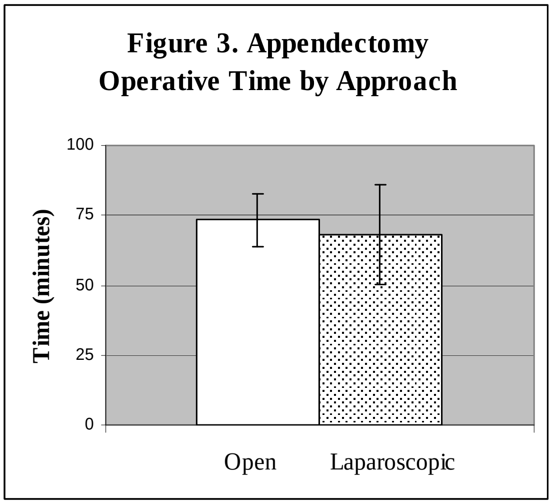
Between 1992 and 2007, 60 appendectomies (44 open, 14 laparoscopic, and two laparoscopic-to-open conversions) were performed on patients with singleton pregnancies at our institution. As previously mentioned, the two conversion cases will be excluded, leaving 58 cases for the appendectomy subgroup analysis. Pathology was available for all 58 cases; we report at 37.9% (n=22) rate of false-positive appendicitis.

The 44 open appendectomies were performed throughout all three trimesters: 23% (n=10) in the first, 41% (n=18) in the second, and 36% (n=16) in the third trimester. The 14 laparoscopic appendectomies were performed at earlier gestational ages: 57% (n=8) occurred in the first trimester, 36 (n=5) in the second, and 7% (n=1) in the third trimester (Figure 2).

Figure 2. Gestational Age at Time of Appendectomy



There was no difference in the average age or BMI of the patients undergoing open and laparoscopic appendectomy (Table 2). There was, however, a statistically significant difference in the mean gestational age at the time of surgery; with open appendectomies being performed on patients with more advanced gestational age (20.5 ± 8.2 weeks, n= 44 vs. 12.7 ± 7.9 weeks, n=14, p <0.05, pooled-variance t test). The mean operative time was similar for open (73.4 ± 31.3 min, n=44) and laparoscopic (68.0 ± 30.9 min, n=14) appendectomies (p=0.57, pooled-variance t test) (Figure 3). There was one open appendectomy postoperative complication (2.3%), a bowel perforation during lysis of adhesions. There were no postoperative complications noted among the



laparoscopic appendectomies. The average postoperative day of discharge was later for open (4.1 ± 2.4 days, n=44) than laparoscopic (1.9 ± 0.9 days, n=14) appendectomies (*p* <0.05, Welch-Satterthwaite t test, Table 2).

The average number of weeks between the surgery and delivery was lower for open (15.8 ± 9.8 weeks, n=36) than laparoscopic (24.3 ± 7.9 weeks, n=11) appendectomies (*p* <0.05, pooled-variance t test). However, the gestational age at delivery was similar for open (37.2 ± 5.6 weeks, n=36) and laparoscopic (37.8 ± 3.5 weeks, n=11) appendectomy (*p*= 0.72, pooled-variance t test, Table 2).

	Open			Laparoscopic				
	Mean	n	S.D.	Mean	n	S.D.	*p*- value	Method
Maternal Age	25.8 years	44	6.7	26.1 years	14	4.5	NS[A]	Pooled-variance t test
Body Mass Index (BMI)	27.8	43	5.8	28.8	14	4.3	NS	Pooled-variance t test
Gestational Age at Surgery	20.5 weeks	44	8.2	12.7 weeks	14	7.9	<0.05	Pooled-variance t test
Operative Time	73.4 min	44	31.3	68.0 min	14	30.9	NS	Pooled-variance t test
Total Length of Stay	4.9 days	44	3.0	2.2 days	14	1.0	<0.05	Welch-Satterthwaite t test
Post-Operative Length of Stay	4.1 days	44	2.4	1.9 days	14	0.9	<0.05	Welch-Satterthwaite t test
Gestational Age at Delivery	37.2 weeks	36	5.6	37.8 weeks	11	3.5	NS	Pooled-variance t test
Time Between Surgery and Delivery	15.8 weeks	36	9.8	24.3 weeks	11	7.9	<0.05	Pooled-variance t test
Birth Weight	2872 grams	28	803	3122 grams	11	803	NS	Pooled-variance t test
1 min Apgar	7.5	33	2.6	8.5	11	1.2	NS	Welch-Satterthwaite t test
5 min Apgar	8.2	33	1.9	8.9	11	0.3	<0.05	Welch-Satterthwaite t test
Intraoperative Complication	2.3%	1/44		0.0%	0/14		NS	Fisher's exact test
Postoperative Complication	45.5%	20/44		7.1%	1/14		<0.05	Chi-square test
Postoperative Contractions	15.9%	7/44		0.0%	0/14		NS	Fisher's exact test
Vaginal Delivery	77.8%	28/36		54.6%	6/11		NS	Fisher's exact test
Preterm Delivery	20.0%	7/35		18.2%	2/11		NS	Fisher's exact test
Low Birth Weight	17.9%	5/28		9.1%	1/11		NS	Fisher's exact test
Very Low Birth Weight	10.7%	3/28		9.1%	1/11		NS	Fisher's exact test

Table 2. Comparison of open and laparoscopic appendectomy during pregnancy by maternal and fetal parameters.
[A] Not statistically significant

The postoperative complication rate was significantly higher for open (45%, n=20) than laparoscopic (7%, n=1) appendectomies ($p < 0.05$, chi-square test). Among open appendectomies, 20 patients experienced a total of 23 postoperative complications. The most common postoperative complication was contractions, (16%, n=7), followed by preterm delivery (9%, n=4), ileus lasting greater than four days (5%, n=2), wound infection (5%, n=2), acute respiratory distress syndrome (2%, n=1), deep vein thrombosis (2%, n=1), and pruritis and epidermal erythema attributed to a drug allergy (2%, n=1). Five patients were readmitted after open appendectomies; causes for readmission included wound infection (2%, n=1), gallstone pancreatitis (2%, n=1), partial small bowel obstruction (2%, n=1), and nausea and vomiting (5%, n=2). Among the laparoscopic appendectomies, the sole postoperative complication was a wound abscess diagnosed two weeks postoperatively and treated on an outpatient basis.

Fetal outcomes between open and laparoscopic appendectomy patients were equivocal. The only statistically significant difference was in the five minute Apgar score after open (8.2 ± 1.9, n=33) and laparoscopic (8.9 ±0.3, n=11) appendectomy, however the clinical significance between the two values is debatable. There were no important differences between birth weights, one minute Apgars, and preterm delivery rates. Breathing assistance was required for 10% (n=3) of the open appendectomy infants; the three cases included a needle decompression for left pneumothorax, the use of continuous positive airway pressure (CPAP) for four hours, and intubation for one day. Breathing assistance was not needed for any laparoscopy-associated infants (p=0.56, Fisher's exact test). There are two fetal losses to report, both in patients who had open appendectomies, though their occurrence was not statistically significant. The first patient was 23 years old and underwent an open appendectomy at 11 weeks gestational age. She spontaneously aborted on postoperative day 8; fetal pathology revealed no abnormalities. The second patient was 36 years old and delivered a stillborn 13 weeks postoperatively, at 35 weeks gestational age. These two fetal losses, along with all fetal outcomes of open appendectomy patients, are outlined in Table 3. The fetal outcomes for all fourteen laparoscopic appendectomies are summarized in Table 4.

Patient	Year	Age	Gestational Age (weeks)	Operative Time (min)	Pathology	Obstetric Outcome	Birth Weight (g)	Apgars (1, 5 min)
1	1992	20	20	130	Appendicitis	NSVD at 39 weeks	3543	8, 9
2	1992	22	36	75	Appendicitis	NSVD at 36 weeks	2750	7, 8
3	1992	23	23	40	Appendicitis	NSVD at 39 weeks	*Unknown* [A]	*Unknown*
4	1992	24	27	50	Negative	NSVD at 28 weeks	1020	5, 7
5	1992	26	15	100	Negative	NSVD at 40 weeks	*Unknown*	*Unknown*
6	1992	26	22	80	Negative	Stillbirth at 35 weeks	N/A	N/A
7	1993	25	25	130	Appendicitis	C/S at 41 weeks[B]	*Unknown*	*8, 9*
8	1993	30	32	80	Appendicitis	C/S at 32 weeks	1531	1, 4
9	1994	17	9	80	Appendicitis	*Unknown*	*Unknown*	*Unknown*
10	1994	17	21	75	Negative	NSVD at 39 weeks	3020	9, 9
11	1994	17	29	135	Appendicitis	C/S at 29 weeks	1445	2, 4
12	1994	26	22	65	Negative	NSVD at 39 weeks	2750	9, 9
13	1995	15	10	35	Appendicitis	*Unknown*	*Unknown*	*Unknown*
14	1995	16	24	60	Negative	NSVD at 42 weeks	3260	9, 9
15	1996	29	22	60	Negative	NSVD at 42 weeks	4535	6, 8
16	1997	23	11	40	Negative	SAB at 12 weeks	N/A	N/A
17	1997	29	17	40	Negative	NSVD at 41 weeks	3010	8, 9
18	1998	30	29	60	Appendicitis	NSVD at 38 weeks	3630	8, 9
19	1998	31	11	120	Appendicitis	*Unknown*	*Unknown*	*Unknown*
20	1998	39	14	45	Appendicitis	NSVD at 41 weeks	3101	8, 7
21	1999	19	27	65	Appendicitis	*Unknown*	*Unknown*	*Unknown*
22	1999	21	30	30	Appendicitis	NSVD at 41 weeks	3040	9, 9
23	1999	26	17	80	Appendicitis	NSVD at 40 weeks	3005	9, 9
24	1999	29	27	85	Appendicitis	*Unknown*	*Unknown*	*Unknown*
25	1999	35	13	65	Appendicitis	NSVD at 36 weeks	*Unknown*	9, 9
26	2000	18	10	150	Negative	C/S at 39 weeks	*2950*	9, 9
27	2000	22	10	45	Negative	*Unknown*	*Unknown*	*Unknown*
28	2000	22	16	40	Negative	NSVD at 37 weeks	*Unknown*	9, 9
29	2000	27	13	85	Negative	NSVD at 38 weeks	*Unknown*	9, 9
30	2000	28	6	55	Appendicitis	*Unknown*	*Unknown*	*Unknown*
31	2000	28	22	65	Appendicitis	NSVD at 39 weeks	3360	9, 9
32	2000	35	27	85	Negative	NSVD at 39 weeks	2985	2, 5
33	2000	38	12	45	Appendicitis	NSVD at 38 weeks	2880	9, 9
34	2001	20	17	60	Appendicitis	NSVD at 39 weeks	3200	9, 9
35	2001	26	22	40	Appendicitis	NSVD at 36 weeks	2780	8, 9
36	2002	24	5	45	Negative	NSVD at 40 weeks	3330	9, 9
37	2002	37	28	65	Negative	C/S at 38 weeks	3080	8, 9
38	2002	41	34	50	Appendicitis	NSVD at 40 weeks	3840	9, 9
39	2003	38	24	150	Negative	*Unknown*	*Unknown*	*Unknown*
40	2004	29	34	95	Appendicitis	NSVD at 37 weeks	2450	9, 9
41	2005	24	25	65	Appendicitis	NSVD at 27 weeks	928	0, 1
42	2006	18	25	65	Appendicitis	NSVD at 40 weeks	2930	7, 9
43	2007	19	30	105	Appendicitis	NSVD at 38 weeks	2560	9, 9
44	2007	28	10	95	Appendicitis	C/S at 40 weeks	3500	9, 9

Table 3. Fetal outcome among open appendectomy patients

[A] Information unavailable

[B] Cesarean section = C/S

Patient	Year	Age	Gestational Age (weeks)	Operative Time (min)	Pathology	Obstetric Outcome	Birth Weight (g)	Apgars (1, 5 min)
1	1998	25	6	80	Negative	NSVD at 28 weeks	1116	5, 8
2	1999	23	10	110	Appendicitis	NSVD at 40 weeks	4054	8, 9
3	2001	31	5	60	Negative	C/S at 38 weeks[A]	2680	9, 9
4	2003	26	13	65	Appendicitis	NSVD at 39 weeks	3444	9, 9
5	2003	29	8	90	Appendicitis	C/S at 40 weeks	3505	8, 9
6	2004	29	17	55	Appendicitis	NSVD at 39 weeks	3130	9, 9
7	2005	35	9	22	Negative	NSVD at 36 weeks	3570	9, 9
8	2005	22	6	100	Appendicitis	C/S at 39 weeks	3520	9, 9
9	2005	30	28	25	Negative	C/S at 37 weeks	2612	9, 9
10	2006	17	18	90	Appendicitis	*Unknown* [B]	*Unknown*	*Unknown*
11	2007	22	23	75	Appendicitis	C/S at 40 weeks	2920	9, 9
12	2007	26	5	15	Negative	*Unknown*	*Unknown*	*Unknown*
13	2007	25	24	60	Appendicitis	NSVD at 40 weeks	3790	9, 9
14	2007	26	6	105	Appendicitis	*Unknown*	*Unknown*	*Unknown*

Table 4. Fetal outcome among laparoscopic appendectomy patients

[A] Cesarean section = C/S

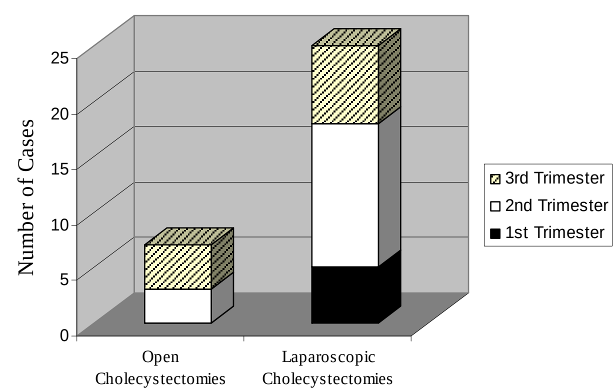
[B] Lost to follow-up

Cholecystectomies

During the years 1992 to 2007, our institution performed 31 cholecystectomies (five open, 25 laparoscopic, and one laparoscopic-to-open conversion) on patients with singleton pregnancies. After the exclusion of the one conversion case, thirty cases remained for cholecystectomy subgroup analysis.

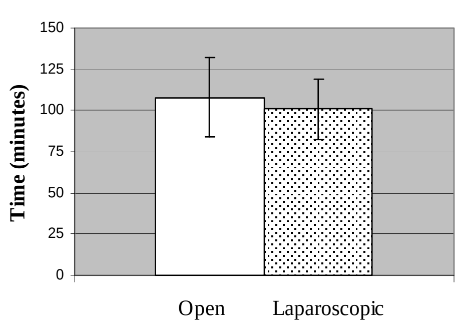
Of the five open cholecystectomies, 60% (n=3) were performed in the second trimester, and 40% (n=2) in the third trimester. The 25 laparoscopic cholecystectomies were performed throughout all three trimesters, with 20% (n=5) during the first trimester, 52% (n=13) in the second trimester, and 28% (n=7) in the third trimester (Figure 5).

Figure 5. Gestational Age at Time of Cholecystectomy



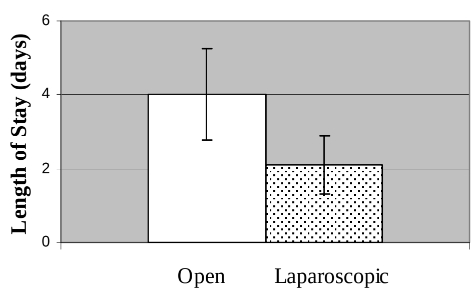
There was no difference between age and BMI for open and laparoscopic cholecystectomy patients (Table 2). The gestational age at the time of surgery was higher for open (24.4 ± 6.1 weeks, n=5) than for laparoscopic (19.1 ± 6.6 weeks, n=25) cholecystectomy patients, but did not reach statistical significance (*p*=0.11, pooled-variance t test). The gestational age at delivery and the number of weeks between surgery and delivery were similar, as was the mean operative time for open (108.0 ± 19.2 min, n=5) and laparoscopic (100.8 ± 6.6 min, n=25) cholecystectomies (*p*=0.73, pooled-variance t test) (Figure 6).

Figure 6. Cholecystectomy Operative Time by Approach



One open cholecystectomy patient (20%) had a postoperative complication; the patient exhibited masseter muscle rigidity from succinylcholine administration but was successfully re-intubated. One laparoscopic cholecystectomy patient (4%) had a postoperative complication, a transient dysrhythmia described as a three minute episode of bigeminy which then spontaneously converted to sinus rhythm. The lone statistically significant difference was that the postoperative length of stay was nearly doubled among open (4.0 ± 1.0 days, n=5) cholecystectomy patients as compared to laparoscopic (2.1 ± 1.9 days, n=25) cholecystectomy patients ($p<0.05$, pooled-variance t test) (Figure 7).

Figure 7. Cholecystectomy Post-Operative Length of Stay by Approach



	Open			Laparoscopic				
	Mean	**n**	**S.D.**	**Mean**	**n**	**S.D.**	***p*-value**	**Method**
Maternal Age	26.0 years	5	6.1	25.3 years	25	5.6	NS[A]	Pooled-variance t test
Body Mass Index (BMI)	31.8	5	6.15	31.2	25	10.4	NS	Pooled-variance t test
Gestational Age at Surgery	24.4 weeks	5	6.1	19.1 weeks	25	6.6	NS	Pooled-variance t test
Operative Time	108.0 min	5	19.2	100.8 min	25	44.2	NS	Pooled-variance t test
Total Length of Stay	6.4 days	5	2.5	4.6 days	25	4.8	NS	Pooled-variance t test
Post-Operative Length of Stay	4.0 days	5	1.0	2.1 days	25	1.9	<0.05	Pooled-variance t test
Gestational Age at Delivery	38.4 weeks	5	2.7	38.8 weeks	18	1.7	NS	Pooled-variance t test
Time Between Surgery and Delivery	14.0 weeks	5	8.5	19.6 weeks	18	7.5	NS	Pooled-variance t test
Birth Weight	3105 grams	4	511	3329 grams	15	570	NS	Pooled-variance t test
1 min Apgar	8.6	5	0.5	8.3	17	1.9	NS	Welch-Satterthwaite t test
5 min Apgar	8.8	5	0.4	8.7	17	1.2	NS	Pooled-variance t test
Intraoperative Complication	20.0%	1/5		4.0%	1/25		NS	Fisher's exact test
Postoperative Complication	40.0%	2/5		24.0%	6/25		NS	Fisher's exact test
Postoperative Contractions	20.0%	1/5		4.0%	1/25		NS	Fisher's exact test
Vaginal Delivery	60.0%	3/5		61.1%	11/18		NS	Fisher's exact test
Preterm Delivery	20.0%	1/5		5.26%	1/19		NS	Fisher's exact test
Low Birth Weight	0.0%	0/4		0.0%	0/15			
Very Low Birth Weight	0.0%	0/4		0.0%	0/15			

Table 5. Comparison of open and laparoscopic cholecystectomy during pregnancy by maternal and fetal parameters.
[A] Not statistically significant

Forty percent (n=2) of open cholecystectomy patients presented with a total of three postoperative complications: ARDS (n=1), preterm delivery (n=1), and pruritis and epidermal erythema attributed to a drug allergy (n=1). The sole preterm delivery occurred in a 34 year old who underwent an open cholecystectomy at 34 weeks gestational age; her infant was of normal birth weight (2780g) and had Apgars of 8, 8. Six laparoscopic cholecystectomy patients (24%, n=6) presented with a total of eight postoperative complications, including readmission (n=5), contractions (n=1), and umbilical hernias (n=2) that became symptomatic six weeks and three years postoperatively, respectively. The principle symptoms prompting readmission included nausea, vomiting, and RUQ pain; the symptoms of one patient with two readmissions were attributed to pancreatitis.

Fetal outcomes were similar for the open and laparoscopic cholecystectomy patients; there were no statistical differences between birth weights, Apgar scores at one and five minutes, and preterm delivery rates. No open cholecystectomy infants required breathing assistance, while one infant in the laparoscopic cholecystectomy group was placed on CPAP for the first two days of life. Among the 30 cholecystectomy patients, there were no spontaneous abortions, therapeutic abortions, stillbirths, or perinatal deaths reported. The open and laparoscopic cholecystectomy cases are summarized in Table 6 and Table 7, respectively.

Patient	Year	Age	Gestational Age (weeks)	Operative Time (min)	Obstetric Outcome	Birth Weight (g)	Apgars (1, 5 min)
1	1992	27	17	80	NSVD at 40 weeks	2570	9, 9
2	1992	27	23	110	C/S at 38 weeks[A]	3640	9, 9
3	1992	34	34	100	NSVD at 34 weeks	2780	8, 8
4	1993	25	25	130	C/S at 41 weeks	*Unknown* [B]	8, 9
5	1994	17	23	120	NSVD at 39 weeks	3430	9, 9

Table 6. Fetal outcome among open cholecystectomy patients

[A] Cesarean section = C/S

[B] Lost to follow-up

Patient	Year	Age	Gestational Age (weeks)	Operative Time (min)	Obstetric Outcome	Birth Weight (g)	Apgars (1, 5 min)
1	1992	19	9	135	NSVD at 39 weeks	2840	9, 9
2	1995	18	28	110	NSVD at 37 weeks	3005	9, 9
3	1995	17	23	120	C/S at 39 weeks[A]	3180	9, 9
4	1995	29	28	85	NSVD at 40 weeks	3050	9, 9
5	1997	30	18	110	C/S at 38 weeks	*Unknown* [B]	9, 9
6	1997	29	17	210	C/S at 39 weeks	4595	9, 9
7	1997	31	23	70	NSVD at 39 weeks	3770	9, 9
8	1997	22	16	225	C/S at 39 weeks	*Unknown*	1, 4
9	1997	29	26	90	NSVD at 40 weeks	*Unknown*	*Unknown*
10	1999	26	15	90	*Unknown*	*Unknown*	*Unknown*
11	2000	32	22	50	*Unknown*	*Unknown*	*Unknown*
12	2000	20	8	50	NSVD at 41 weeks	3610	8, 9
13	2001	34	15	105	NSVD at 38 weeks	3840	9, 9
14	2001	31	28	60	NSVD at 42 weeks	3950	8, 9
15	2001	19	18	135	*Unknown*	*Unknown*	*Unknown*
16	2002	31	11	95	C/S at 35 weeks	2955	8, 9
17	2002	32	25	105	C/S at 38 weeks	2870	9, 9
18	2003	18	21	105	*Unknown*	*Unknown*	*Unknown*
19	2004	29	12	80	*Unknown*	*Unknown*	*Unknown*
20	2005	23	10	130	C/S at 39 weeks	3800	9, 9
21	2005	20	13	95	NSVD at 41 weeks	3220	9, 9
22	2007	21	31	60	NSVD at 38 weeks	2610	9, 9
23	2007	23	23	60	*Unknown*	*Unknown*	*Unknown*
24	2007	19	17	40	NSVD at 37 weeks	2640	9, 9
25	2007	31	21	105	*Unknown*	*Unknown*	*Unknown*

Table 7. Fetal outcome among laparoscopic cholecystectomy patients

[A] Cesarean section = C/S

[B] Lost to follow-up

Discussion

Based on the results of this study, we accept our hypothesis that nonobstetric laparoscopy during pregnancy maintains the well-described advantages of laparoscopic surgery and has an equal incidence of maternal and fetal morbidity and mortality as nonobstetric laparotomy during pregnancy.

The observed incidence for appendectomy at YNHH (one in 1,162) falls within the published range of one in 766 to one in 3,000 [24, 47]. Likewise, the observed incidence of cholecystectomy at our institution (one in 2,457) falls within previous estimates of one in 1,666 to one in 5,000 [55].

In comparing the broad categories of laparotomy and laparoscopy in pregnancy, we found that the gestational age at time of surgery was higher in the laparotomy patients. This finding suggests a selection bias on the part of the general surgeon toward open surgery in patients at advanced gestational age. The gestational age at delivery and preterm delivery rate was comparable between the two groups. Our finding of equivalent rates of preterm delivery echoes the findings of the multicenter review by Oelsner *et al* [25] and the Swedish health registry analysis by Reedy *et al* [26].

It is worth emphasizing that the operative time was not statistically different between laparotomy and laparoscopy. This is remarkable because one of the perceived drawbacks of laparoscopy is the expected increase in operative time [16]. As laparoscopic technology advances and more surgeons receive specialized training in minimally invasive techniques, it is conceivable that laparoscopic cases in pregnancy might someday be faster than their open counterparts [66].

Similar to the findings of Barone *et al* [37], laparotomy fared worse than laparoscopy in terms of the rate of postoperative contractions (19.3% vs. 2.2%). The widely accepted benefit of laparoscopic surgery allowing for earlier return to normal activity held true for the pregnant population, as the laparotomy patients had a longer total length of stay (5.5 vs. 3.7 days), and a longer postoperative length of stay (4.5 vs. 2.2 days) than the laparoscopic patients. While the laparotomy-associated infants had a lower average birth weight (2902 vs. 3324 grams), there was no difference in the rate of low-birth-weight infants. The average increased weight of 422 grams seen in the laparoscopy-associated infants may or may not be clinically significant. There were no statistically significant differences in Apgar scores, spontaneous abortion, stillbirth, or perinatal death. The amalgamation of these findings support the opinion of Affeck *et al* [24] that laparoscopy is preferential to laparotomy during pregnancy.

Appendectomies comprised 56% of the cases analyzed above, supporting the previously published assertion that appendectomy is the most common nonobstetric surgery performed during pregnancy [2]. The appendectomy subgroup analysis produced similar results to the at-large group, with a few notable exceptions. In contrast to the comparison between laparoscopy and laparotomy in general, there was no statistically significant difference in birth weight or the rate of postoperative contractions among the two appendectomy groups. The infants of laparotomy patients had a lower five minute Apgar score (8.2 vs. 8.9), but this is likely clinically insignificant because an Apgar score of 8 or higher is considered normal.

Analysis of cholecystectomy cases (5 open, 25 laparoscopic) revealed just one difference between the open and laparoscopy groups; the postoperative length of stay averaged 1.9 days longer after open cholecystectomy (4.0 vs. 2.1 days). While the values of the other outcome parameters for cholecystectomies exhibited trends similar to those seen in the general laparotomy and laparoscopy groups (lower birth weight, increased postoperative contraction rate, and increased intra- and postoperative complication rates among open cholecystectomy patients), the small sample size did not allow for these values to reach statistical significance.

The cases included in our analysis have not previously been published; specifically, none were included in the review of cholecystectomy during pregnancy in Connecticut by Barone *et al* [67]. The results of this single institution case series are limited to pregnant women undergoing nonobstetric intraabdominal surgery at Yale-New Haven Hospital, and may not generalize to other institutions. We are aware of the potential bias of our study based on its retrospective design, including the fact that we are completely dependent on the accuracy of the medical record. While a large prospective trial would add strength to the slowly-accumulating scientific evidence supporting the use of laparoscopic surgery during pregnancy, the rarity of the situation and the ethics of withholding surgery that is emerging as the standard of care (as is the case in cholecystectomy) from pregnant patients make the possibility of a large prospective trial unlikely.

Patients with fetuses of viable gestational age should receive an obstetrics consultation and should undergo surgery at an institution with facilities capable of caring for the premature infant, should preterm delivery occur [24, 39]. We conclude with guidelines on how to approach laparoscopy during pregnancy.

General considerations for laparoscopy in pregnancy

Laparoscopic surgery during pregnancy mandates special attention. With the following considerations in place, laparoscopy can be performed with minimal maternal and fetal morbidity and mortality. Standard operative patient positioning used in nongravid patients is not always appropriate for gravid patients; therefore adjustments should be made according to the patient's gestational age. During the first trimester, the standard supine position is suitable. During the second and third trimester, the enlarged uterus compresses the inferior vena cava; this compromise of venous return can impact the maternal cardiac output and, subsequently, uterine blood flow. To maximize venous return, the uterus can be displaced to the left by placing the patient in a left lateral decubitus position [19, 68].

The use of routine intraoperative fetal heart monitoring is generally considered unnecessary [24, 40]. When intraoperative fetal heart monitoring is desired during laparoscopy, transvaginal ultrasound is recommended over transabdominal ultrasound in order to maintain a continuous signal during abdominal insufflation and to minimize the risk of contamination to the operative field [16, 61]. In contrast to intraoperative fetal heart monitoring, pre- and postoperative fetal heart monitoring are generally considered indicated for all pregnancies of viable gestational age [69].

Similar to nongravid patients, capnography is used to monitor maternal acid/base status during laparoscopy. Initially, controversy existed as to whether capnography adequately represented maternal arterial carbon dioxide pressure ($PaCO_2$) during laparoscopy. During normal pregnancy, the diaphragm elevates and decreases total lung capacity, which in turn decreases expiratory reserve volume, residual volume, and functional residual capacity [10]. In contrast, tidal volume increases and minute ventilation increases up to 1.5 times its normal level, causing a physiologic respiratory alkalosis [70, 71]. Concerns have been expressed that the carbon dioxide pneumoperitoneum used in laparoscopic surgery might exacerbate maternal hypercapnia and exaggerate fetal acidosis. Regardless of the surgical approach, the anesthesiologist should be knowledgeable of the normal physiologic changes during pregnancy [72].

Controversy exists as to the appropriateness of using Veress needles in gravid patients, due in part to reports of inadvertent uterine and bowel injuries during trocar insertion. While some surgeons feel comfortable using Veress needles, others recommend the use of the Hasson open technique, or direct vision dissecting ports [16, 73]. Regardless of the method chosen for port placement, there is consensus that increasing gestational age necessitates adjustments in port site locations. The gravid uterus usually reaches the level of the umbilicus at 20 weeks gestation, making a peri-umbilical port site hazardous in the second and third trimester of pregnancy [10]. The recommended site for the initial camera port during the second and third trimester ranges from supra-umbilical, to sub-xiphoid, to the left or right midclavicular line three centimeters below the costal margin [72]. The remaining trocars should be placed under direct vision, as in all laparoscopic cases, and their port sites may also require cephalad displacement in order to avoid the gravid uterus [57].

Carbon dioxide is used in laparoscopy for its rapid absorption, high solubility, and rapid clearance, however, concerns have been raised over the effect of carbon dioxide pneumoperitoneum during pregnancy [74]. A study of pregnant ewes published in 1994 by Hunter *et al* [41] demonstrated that carbon dioxide pneumoperitoneum at 15mmHg induced maternal hypercapnia and acidosis, and fetal hypercapnia, acidosis, tachycardia, and hypertension. In addition, the authors stated that capnography lagged up to one hour behind in reflecting peak maternal $PaCO_2$ levels, implying that capnography hindered prompt ventilatory correction of hypercapnia. With these findings, the authors recommended the use of serial blood gases in all patients undergoing laparoscopy during pregnancy [41]. The abnormal maternal and fetal values corrected after desufflation; while Hunter *et al* admitted that the clinical significance of these physiologic changes during pneumoperitoneum was unknown, Comitalo *et al* [75] actively questioned the clinical significance of the transient maternal hypercapnia and fetal acidosis, stating, "as the vast majority of pregnant patients are young and healthy, the acid-base changes occasionally seen with CO_2 pneumoperitoneum probably pose no significant risk to the mother or fetus."

In 2000, Bhavani-Shankar *et al* [76] published findings from a prospective study of eight human laparoscopic surgeries during pregnancy, demonstrating no significant differences in mean maternal end-tidal carbon dioxide pressure, $PaCO_2$, and pH during laparoscopic surgery. The authors concluded that capnography accurately reflected maternal $PaCO_2$ (within 3.1 mmHg) and adequately guided ventilation during laparoscopic surgery [76]. The acquisition of serial blood gases is now generally considered unnecessary, and mechanical ventilation is believed to effectively maintain normal end-tidal carbon dioxide pressure in pregnant laparoscopy patients [5].

The use of alternative gases to carbon dioxide for the achievement of pneumoperitoneum has been advocated based on favorable results observed in animal studies. Hunter *et al* [41] demonstrated that pneumoperitoneum in and of itself is not deleterious; a nitrous oxide pneumoperitoneum in pregnant ewes did not cause the fetal hypercapnia or fetal hypertension observed in a carbon dioxide pneumoperitoneum. Likewise, studies in pregnant ewes by Curet *et al* [77] show that a helium pneumoperitoneum has a lower incidence of maternal and fetal acidosis.

In addition to concerns regarding the acid/base effects of carbon dioxide pneumoperitoneum, it has been speculated that heightened intraabdominal pressure induced by pneumoperitoneum decreases uterine blood flow, which in turn decreases placental perfusion and causes fetal hypoxia. This concern remains hypothetical; these sequelae have not been shown in humans [39]. The act of coughing and the Valsalva maneuver increase intraabdominal pressure beyond that of 15 mmHg, but these physiologic acts have not been shown to correlate with fetal distress. Likewise, some argue that the increased intraabdominal pressure generated during pneumoperitoneum has no clinical significance for the fetus [57]. Most surgeons recommend using a lower-than-normal maximum pressure to achieve pneumoperitoneum during pregnancy; the pressure ranges most frequently utilized during laparoscopic surgery during pregnancy are 10-12mmHg or 12-15mmHg, though one paper described using 6-10mmHg to perform cholecystectomies in gravid patients [17]. The benefits of minimizing pneumoperitoneal pressures must be weighed against the risk of impaired visualization, which may lengthen operative time and increase the risk of iatrogenic injury [24].

The risk of thromboembolic events is increased fivefold during pregnancy, due to the hypercoagulable state induced by increased levels of fibrinogen complexes and increased concentrations of clotting factors II, V, VII, VIII, IX, X, and XII [10, 42]. Pneumoperitoneum further exacerbates lower extremity venous stasis, therefore pneumatic compression stockings are crucial, and heparin prophylaxis may be indicated until the patient is fully mobilized [9, 41].

Conclusion

The data presented here examines relative outcomes between 46 open and 57 laparoscopic nonobstetric surgeries during pregnancy. Our data demonstrate no difference in operative time, mean gestational age at delivery, or the rate of fetal loss between open and laparoscopic patients. We found the postoperative length of stay associated with laparoscopy to be half that associated with laparotomy. This shortened length of stay is beneficial to the patient both in terms of decreased cost of hospitalization and decreased risk of hospital-acquired infections and other such postoperative complications. The postoperative complication rate associated with laparoscopy was less than half that associated with laparotomy during pregnancy. Therefore, our data demonstrate that laparoscopy during pregnancy confers a statistically significant and demonstrable advantage compared to laparotomy during pregnancy because of shortened maternal hospitalization and decreased incidence of postoperative complications.

References

1. Kammerer, W., *Nonobstetric surgery during pregnancy*. Med Clin North Am, 1979. **63**(6): p. 1157-64.
2. Kort, B., V.L. Katz, and W.J. Watson, *The effect of nonobstetric operation during pregnancy*. Surg Gynecol Obstet, 1993. **177**(4): p. 371-6.
3. Malangoni, M.A., *Gastrointestinal surgery and pregnancy*. Gastroenterol Clin North Am, 2003. **32**(1): p. 181-200.
4. McKellar, D., et al., *Cholecystectomy during pregnancy without fetal loss*. Surg Gynecol Obstet, 1992. **174**(6): p. 465-8.
5. Fatum, M. and N. Rojansky, *Laparoscopic surgery during pregnancy*. Obstet Gynecol Surv, 2001. **56**(1): p. 50-9.
6. Gurbuz, A.T. and M.E. Peetz, *The acute abdomen in the pregnant patient. Is there a role for laparoscopy?* Surg Endosc, 1997. **11**(2): p. 98-102.
7. Kilpatrick, C.C. and M. Monga, *Approach to the acute abdomen in pregnancy*. Obstet Gynecol Clin North Am, 2007. **34**(3): p. 389-402, x.
8. Melnick, D.M., W.L. Wahl, and V.K. Dalton, *Management of general surgical problems in the pregnant patient.* Am J Surg, 2004. **187**(2): p. 170-80.
9. Halkic, N., et al., *Laparoscopic management of appendicitis and symptomatic cholelithiasis during pregnancy*. Langenbecks Arch Surg, 2006. **391**(5): p. 467-71.
10. Cunningham FG, L.K., Bloom SL, Hauth JC, Gilstrap III LC, Wenstrom KD, *Williams Obstetrics*. 22nd ed. 2005, New York: McGraw-Hill Professional.
11. Cohen-Kerem, R., et al., *Pregnancy outcome following non-obstetric surgical intervention.* Am J Surg, 2005. **190**(3): p. 467-73.
12. Mazze, R.I. and B. Kallen, *Reproductive outcome after anesthesia and operation during pregnancy: a registry study of 5405 cases.* Am J Obstet Gynecol, 1989. **161**(5): p. 1178-85.
13. Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Publication #0023, *Guidelines for Diagnosis, Treatment, and Use of Laparoscopy for Surgical Problems during Pregnancy*. 2007. [Available at: http://www.sages.org/sg_pub23.html Accessed on November 21, 2007].
14. Chamogeorgakis, T., et al., *Laparoscopic cholecystectomy during pregnancy: three case reports.* JSLS, 1999. **3**(1): p. 67-9.
15. F. Gary Cunningham, K.L.L., Steven L. Bloom, John C. Hauth, Larry C. Gilstrap III, Katharine D. Wenstrom, *Williams Obstetrics*. 22nd ed. 2005, New York: McGraw-Hill Professional.
16. Curet, M.J., et al., *Laparoscopy during pregnancy*. Arch Surg, 1996. **131**(5): p. 546-50; discussion 550-1.
17. Glasgow, R.E., et al., *Changing management of gallstone disease during pregnancy*. Surg Endosc, 1998. **12**(3): p. 241-6.
18. Gadacz, T. and M. Talamini, *Traditional versus laparoscopic cholecystectomy*. Am J Surg, 1991. **161**(3): p. 336-8.
19. Al-Fozan, H. and T. Tulandi, *Safety and risks of laparoscopy in pregnancy*. Curr Opin Obstet Gynecol, 2002. **14**(4): p. 375-9.

20. Sainsbury, D.C., et al., *Laparoscopic radical nephrectomy in first-trimester pregnancy.* Urology, 2004. **64**(6): p. 1231 e7-8.
21. Griffiths, J., et al., *Laparoscopic splenectomy for the treatment of refractory immune thrombocytopenia in pregnancy.* J Obstet Gynaecol Can, 2005. **27**(8): p. 771-4.
22. Reedy, M.B., et al., *Laparoscopy during pregnancy. A survey of laparoendoscopic surgeons.* J Reprod Med, 1997. **42**(1): p. 33-8.
23. Andreoli, M., et al., *Laparoscopic surgery during pregnancy.* J Am Assoc Gynecol Laparosc, 1999. **6**(2): p. 229-33.
24. Affleck, D.G., et al., *The laparoscopic management of appendicitis and cholelithiasis during pregnancy.* Am J Surg, 1999. **178**(6): p. 523-9.
25. Oelsner, G., et al., *Pregnancy outcome after laparoscopy or laparotomy in pregnancy.* J Am Assoc Gynecol Laparosc, 2003. **10**(2): p. 200-4.
26. Reedy, M.B., B. Kallen, and T.J. Kuehl, *Laparoscopy during pregnancy: a study of five fetal outcome parameters with use of the Swedish Health Registry.* Am J Obstet Gynecol, 1997. **177**(3): p. 673-9.
27. Rizzo, A.G., *Laparoscopic surgery in pregnancy: long-term follow-up.* J Laparoendosc Adv Surg Tech A, 2003. **13**(1): p. 11-5.
28. Thomas, S.J. and P. Brisson, *Laparoscopic appendectomy and cholecystectomy during pregnancy: six case reports.* JSLS, 1998. **2**(1): p. 41-6.
29. Steinbrook, R.A., D.C. Brooks, and S. Datta, *Laparoscopic surgery during pregnancy.* Am J Surg, 1997. **174**(2): p. 222.
30. Gouldman, J.W., et al., *Laparoscopic cholecystectomy in pregnancy.* Am Surg, 1998. **64**(1): p. 93-7; discussion 97-8.
31. Moreno-Sanz, C., et al., *Laparoscopic appendectomy during pregnancy: between personal experiences and scientific evidence.* J Am Coll Surg, 2007. **205**(1): p. 37-42.
32. Palanivelu, C., et al., *Safety and efficacy of laparoscopic surgery in pregnancy: experience of a single institution.* J Laparoendosc Adv Surg Tech A, 2007. **17**(2): p. 186-90.
33. Sen, G., J.S. Nagabhushan, and V. Joypaul, *Laparoscopic cholecystectomy in third trimester of pregnancy.* J Obstet Gynaecol, 2002. **22**(5): p. 556-7.
34. Schwartzberg, B.S., J.A. Conyers, and J.A. Moore, *First trimester of pregnancy laparoscopic procedures.* Surg Endosc, 1997. **11**(12): p. 1216-7.
35. Sungler, P., et al., *Laparoscopic cholecystectomy and interventional endoscopy for gallstone complications during pregnancy.* Surg Endosc, 2000. **14**(3): p. 267-71.
36. Wu, J.M., et al., *Laparoscopic appendectomy in pregnancy.* J Laparoendosc Adv Surg Tech A, 2005. **15**(5): p. 447-50.
37. Barone, J.E., et al., *Outcome study of cholecystectomy during pregnancy.* Am J Surg, 1999. **177**(3): p. 232-6.
38. Pucci, R.O. and R.W. Seed, *Case report of laparoscopic cholecystectomy in the third trimester of pregnancy.* Am J Obstet Gynecol, 1991. **165**(2): p. 401-2.
39. Barnes, S.L., et al., *Laparoscopic appendectomy after 30 weeks pregnancy: report of two cases and description of technique.* Am Surg, 2004. **70**(8): p. 733-6.

40. O'Rourke, N. and B.S. Kodali, *Laparoscopic surgery during pregnancy.* Curr Opin Anaesthesiol, 2006. **19**(3): p. 254-9.
41. Hunter, J.G., L. Swanstrom, and K. Thornburg, *Carbon dioxide pneumoperitoneum induces fetal acidosis in a pregnant ewe model.* Surg Endosc, 1995. **9**(3): p. 272-7; discussion 277-9.
42. Lachman, E., et al., *Pregnancy and laparoscopic surgery.* J Am Assoc Gynecol Laparosc, 1999. **6**(3): p. 347-51.
43. de Perrot, M., et al., *Laparoscopic appendectomy during pregnancy.* Surg Laparosc Endosc Percutan Tech, 2000. **10**(6): p. 368-71.
44. Upadhyay, A., et al., *Laparoscopic management of a nonobstetric emergency in the third trimester of pregnancy.* Surg Endosc, 2007. **21**(8): p. 1344-8.
45. Geisler, J.P., et al., *Non-gynecologic laparoscopy in second and third trimester pregnancy: obstetric implications.* JSLS, 1998. **2**(3): p. 235-8.
46. Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Publication #0023, *Guidelines for laparoscopic surgery during pregnancy*. 2000. [Available at: http://www.sages.org/sg_pub23.html Accessed on February 2, 2007].
47. McGory, M.L., et al., *Negative appendectomy in pregnant women is associated with a substantial risk of fetal loss.* J Am Coll Surg, 2007. **205**(4): p. 534-40.
48. EA, B., *Perforative appendicitis complicating pregnancy.* JAMA, 1908. **51**: p. 1310-1313.
49. Mazze, R.I. and B. Kallen, *Appendectomy during pregnancy: a Swedish registry study of 778 cases.* Obstet Gynecol, 1991. **77**(6): p. 835-40.
50. Hale, D., et al., *Appendectomy: a contemporary appraisal.* Ann Surg, 1997. **225**(3): p. 252-61.
51. Wallace, C., et al., *Influence of Imaging on the Negative Appendectomy Rate in Pregnancy.* J Gastrointest Surg, 2008. **12**(1): p. 46-50.
52. Rojansky, N., A. Shushan, and M. Fatum, *Laparoscopy versus laparotomy in pregnancy: a comparative study.* J Am Assoc Gynecol Laparosc, 2002. **9**(1): p. 108-10.
53. Carver, T.W., et al., *Appendectomy during early pregnancy: what is the preferred surgical approach?* Am Surg, 2005. **71**(10): p. 809-12.
54. Lanzafame, R.J., *Laparoscopic cholecystectomy during pregnancy.* Surgery, 1995. **118**(4): p. 627-31; discussion 631-3.
55. Bani Hani, M., *Laparoscopic surgery for symptomatic cholelithiasis during pregnancy.* Surg Laparosc Endosc Percutan Tech, 2007. **17**(6): p. 482-6.
56. Dixon, N.P., D.M. Faddis, and H. Silberman, *Aggressive management of cholecystitis during pregnancy.* Am J Surg, 1987. **154**(3): p. 292-4.
57. Wishner, J.D., et al., *Laparoscopic cholecystectomy in pregnancy. A report of 6 cases and review of the literature.* Surg Endosc, 1996. **10**(3): p. 314-8.
58. Stepp, K. and T. Falcone, *Laparoscopy in the second trimester of pregnancy.* Obstet Gynecol Clin North Am, 2004. **31**(3): p. 485-96, vii.
59. Weber, A., et al., *Laparoscopic cholecystectomy during pregnancy.* Obstet Gynecol, 1991. **78**(5 Pt 2): p. 958-9.
60. Arvidsson, D. and E. Gerdin, *Laparoscopic cholecystectomy during pregnancy.* Surg Laparosc Endosc, 1991. **1**(3): p. 193-4.

61. Graham, G., L. Baxi, and T. Tharakan, *Laparoscopic cholecystectomy during pregnancy: a case series and review of the literature.* Obstet Gynecol Surv, 1998. **53**(9): p. 566-74.
62. Rollins, M.D., K.J. Chan, and R.R. Price, *Laparoscopy for appendicitis and cholelithiasis during pregnancy: a new standard of care.* Surg Endosc, 2004. **18**(2): p. 237-41.
63. Allen, J., T. Helling, and M. Langenfeld, *Intraabdominal surgery during pregnancy.* Am J Surg, 1989. **158**(6): p. 567-9.
64. Buser, K.B., *Laparoscopic surgery in the pregnant patient--one surgeon's experience in a small rural hospital.* JSLS, 2002. **6**(2): p. 121-4.
65. Friedman, J.D., et al., *Pneumoamnion and pregnancy loss after second-trimester laparoscopic surgery.* Obstet Gynecol, 2002. **99**(3): p. 512-3.
66. Conron, R.W., Jr., et al., *Laparoscopic procedures in pregnancy.* Am Surg, 1999. **65**(3): p. 259-63.
67. Barone, J.E., *Personal Communication*. January 24, 2008.
68. Steinbrook, R.A., *Anaesthesia, minimally invasive surgery and pregnancy.* Best Pract Res Clin Anaesthesiol, 2002. **16**(1): p. 131-43.
69. Visser, B.C., et al., *Safety and timing of nonobstetric abdominal surgery in pregnancy.* Dig Surg, 2001. **18**(5): p. 409-17.
70. Amos, J.D., et al., *Laparoscopic surgery during pregnancy.* Am J Surg, 1996. **171**(4): p. 435-7.
71. Steinbrook, R.A., D.C. Brooks, and S. Datta, *Laparoscopic cholecystectomy during pregnancy. Review of anesthetic management, surgical considerations.* Surg Endosc, 1996. **10**(5): p. 511-5.
72. Lemaire, B.M. and W.F. van Erp, *Laparoscopic surgery during pregnancy.* Surg Endosc, 1997. **11**(1): p. 15-8.
73. Curet, M.J., *Special problems in laparoscopic surgery. Previous abdominal surgery, obesity, and pregnancy.* Surg Clin North Am, 2000. **80**(4): p. 1093-110.
74. Nezhat, F.R., et al., *Laparoscopy during pregnancy: a literature review.* JSLS, 1997. **1**(1): p. 17-27.
75. Comitalo, J.B. and D. Lynch, *Laparoscopic cholecystectomy in the pregnant patient.* Surg Laparosc Endosc, 1994. **4**(4): p. 268-71.
76. Bhavani-Shankar, K., et al., *Arterial to end-tidal carbon dioxide pressure difference during laparoscopic surgery in pregnancy.* Anesthesiology, 2000. **93**(2): p. 370-3.
77. Curet, M.J., et al., *Effects of helium pneumoperitoneum in pregnant ewes.* Surg Endosc, 2001. **15**(7): p. 710-4.