Italian Journal of
Gynæcology & Obstetrics
September 2019 - Vol. 31 - N. 3 - Quarterly - ISSN 2385 - 0868

Non-obstetric surgery during pregnancy: current perspectives and future directions

Chiara Simonetto[1], Simone Garzon[2], Antonio Simone Laganà[2], Jvan Casarin[2], Ricciarda Raffaelli[1], Antonella Cromi[2], Stefano Uccella[3], Fabio Ghezzi[2], Massimo Franchi[1]

[1]Department of Obstetrics and Gynaecology, AOUI Verona, University of Verona, Verona, Italy.
[2]Department of Obstetrics and Gynaecology, "Filippo Del Ponte" Hospital, University of Insubria, Varese, Italy.
[3]Department of Obstetrics and Gynaecology, Ospedale degli Infermi, Biella, Italy.

ABSTRACT

The 1-2% of pregnant women undergo surgery for pregnancy-unrelated conditions, such as appendicitis, cholecystitis, intestinal occlusion or adnexal mass complications. The early diagnosis and treatment of acute abdomen in pregnant woman are complicated by the physiological and anatomical changes of pregnancy, that make more problematic to recognize early signs of emergent conditions. Moreover, the fear of performing potentially dangerous diagnostic procedures contribute to further delay diagnosis and therapies.

In case of acute non-obstetric surgical pathology, conservative management may adversely affect pregnancy outcomes, and surgical intervention should not be deferred only because of the gravid status or the gestational age. Non-obstetric surgery in pregnant patients has been proved to be safe if performed by a team composed by skilled surgeons and obstetricians, and both laparotomic and laparoscopic techniques can be applied if physiological and anatomical changes of pregnancy are considered, and appropriate adjustments are made by the anaesthesiologist.

Nevertheless, in many hospital settings there is still a lack of knowledge, and many obstetricians and surgeons are reluctant to practice surgery in pregnant patients, especially laparoscopy. However, the recent available evidence supports non-obstetric surgery's safety and efficacy, although more data are still needed to make strong recommendations and guidelines.

Keywords: : Surgery; Pregnancy; Laparoscopy; Open surgery; Obstetrics complications

SOMMARIO

Circa l'1-2% delle donne in gravidanza vengono sottoposte a chirurgia per patologia acuta non ostetrica, come l'appendicite, la colecistite, l'occlusione intestinale o le complicanze di una massa annessiale. La diagnosi e il conseguente trattamento precoce dell'addome acuto in gravidanza sono resi più complessi dai cambiamenti che si verificano durante la gravidanza stessa, e che rendono più problematico il riconoscimento dei sintomi e dei segni legati a tali condizioni. Inoltre, la paura di eseguire procedure e test diagnostici potenzialmente dannosi per il feto contribuisce a ritardare ulteriormente la diagnosi.

In caso di patologia acuta non ostetrica, la gestione conservativa proposta in passato si è dimostrata influire negativamente sugli esiti della gravidanza, e l'intervento chirurgico urgente non deve essere rinviato a causa dello stato gravidico o dell'epoca gestazionale. Tale chirurgia ha dimostrato di essere sicura se eseguita da un team altamente specializzato composto da chirurghi e ostetrici esperti, e sia l'approccio laparotomico che laparoscopico possono essere usati senza conseguenze materne o fetali, in particolare quando si considerano i cambiamenti fisiologici e anatomici della gravidanza e gli anestesisti effettuano gli opportuni aggiustamenti.

Tuttavia, anche se le evidenze disponibili supportano la sicurezza della chirurgia, più dati sono necessari per raccomandazioni e linee guida definitive.

Corresponding Author: Simone Garzon
simone.garzon@yahoo.it

DOI: 10.14660/2385-0868-125

INTRODUCTION

Surgical approach represents the gold standard management in several conditions, for benign[1,2] as well as malignant[3,4] diseases. Non-obstetric surgery during pregnancy represents an important concern for both obstetricians and surgeons. According to the National Institute for Health Research, about 1-2% of pregnant women undergo surgery for pregnancy-unrelated conditions, such as appendicitis, cholecystitis, intestinal occlusion or adnexal mass complications[5,6]. Limited evidence is available in the literature, and specific international guidelines have never been raised consensus regarding the surgical management of this particular population[7].

In the last decades, some observational studies showed that surgery during pregnancy is related to specific additional complications, such as premature delivery (8.2%), miscarriage (from 5.8% to 10.5% if surgery took place in the first trimester), and stillbirth (2%)[8]; although in these studies a comparison with women who did not undergo surgery was not performed. Nevertheless, as a result of the surgical progress and the increasingly frequent use of a multidisciplinary approach in the field of obstetrical care[9,10], it is imperative to not deny or delay any necessary urgent surgical treatment in pregnant woman regardless of gestational age, because the delayed treatment seems to adversely affect pregnancy outcomes and foetal health. Conversely, the elective surgery can and should be postponed after the delivery.

In this context, the multidisciplinary approach is mandatory. Before proceeding any surgical intervention in pregnancy, it is necessary for the obstetrician to consult with the general surgeon, especially if the latter is experienced in pregnancy-related surgery and can suggest the best surgical approach to use (laparoscopy or laparotomy).

Moreover, anatomic and physiologic pregnancy-related modifications and the concerns about the foetus may require changes in the anaesthetic and surgical procedures. Therefore, the anaesthesiologist and the neonatologist play both a pivotal role to coordinate the most appropriate management[7].

Lastly, it is important to underline that the clinical characteristics of surgical pathologies during pregnancy may differ from those of a non-pregnant patient, and this could lead to an incorrect or delayed diagnosis that may complicate clinical course of pregnancy.

INDICATIONS FOR SURGERY DURING PREGNANCY

The definition of "acute abdomen" refers generically to any serious acute intra-abdominal condition associated with pain, tenderness, and muscular rigidity, for which an emergent surgical intervention is mandatory[11]. Acute abdomen can occurs in pregnancy and its aetiologies are usually divided into obstetric or non-obstetric causes.

As previously mentioned, non-obstetrical surgical interventions impact up to 2% of all pregnancies[12,13]. The early diagnosis and consequent treatment of acute abdomen in the pregnant woman are complicated by the physiological and anatomical changes occurring during pregnancy, since they make more problematic to recognize early signs of emergent conditions[14]. Moreover, the fear of performing potentially dangerous diagnostic procedures and tests contribute to the high complication rate in this population, making diagnosis and therapies even more delayed.

The most common causes of acute abdomen in pregnancy are appendicitis, cholecystitis, bowel obstruction, adnexal mass complications (ovarian torsion and tumours) and abdominal trauma (**Table 1**).

Table 1
Indications for non-obstetric surgery during pregnancy

Indication	Incidence
Appendicitis	1 in 1500 pregnancies[15,19]
Cholecystitis	1 in 1500 to 1 in 10000 pregnancies[26–28,124]
Bowel obstruction	1 in 1500 to 1 in 3500 pregnancies[34]
Adnexal torsion	1 in 3000 to 1 in 4000 pregnancies[45–47]
Trauma	The 6 to 7% of all pregnancies are complicated by trauma, but the incidence of life-threatening trauma needing emergent intervention is 0.3 to 0.4%[125,126]

Appendicitis. It is the most frequent indication for surgical procedures performed during pregnancy, being suspected in 1/800 pregnancies and confirmed in nearly 1/1000–2000 pregnancies[15–19]. Overall, appendicitis contributes to the 25% of surgical interventions during pregnancy. Many Authors reported different percentages for its frequency throughout the pregnancy, showing no difference in the various trimesters; although a recent cohort analysis found that it occurs more frequently during the second trimester[15].

Clinical characteristics in pregnancy may be confounding. The classical right lower quadrant pain (on Mc Burney's point) and the typical peritoneal irritative reaction (Blumberg's sign) may be altered, especially in the advanced gestational ages, due to the relaxed and stretched abdominal wall. The Adler's sign instead may be useful as much as in non-pregnant women. As pregnancy progresses, it was supposed that the bowel and the appendix get displaced laterally and upward, supporting the previous concept that in pregnancy the pain referred to appendicitis was typically reported in the right upper quadrant[15,20,21]. Nevertheless, recent studies show that the appendix does not migrate up as pregnancy advances, and the right lower quadrant pain is the most common symptom in this population, as in the non-pregnant one[11,18,22].

Imaging plays a key role in the diagnosis of appendicitis. Ultrasound (US) scan has a sensitivity of 67%–100% and a specificity of 83%–96% in detecting appendicitis in pregnant women. Computed Tomography (CT) has been found to have a sensitivity of 86% and specificity of 97% in the same population[23] Magnetic resonance imaging (MRI) is recommended as the second line imaging in case of inconclusive US, due to its low dose of radiation exposure compared to CT[24,25].

The definitive treatment for acute appendicitis is surgery, taking into account that foetal loss occurs in 3%–5% of pregnant patients without perforation and up to 36% in perforated women[14]. Nowadays, laparoscopic appendectomy is preferred instead of open appendectomy.

Cholecystitis. The incidence of cholesterol gallstones abruptly rises during pregnancy, due to the physiological and hormonal changes induced by gravid state. According to recent studies, the incidence of gallstone-related disease in pregnant women is about 0.05 to 0.33%, and only 1.2% of pregnant women with gallstones becomes symptomatic[26–29]. Acute cholecystitis is usually related to the presence of these gallstones. The clinical characteristics do not differ from those of non-pregnant women and clinical diagnosis is usually straightforward with the typically positive Murphy's sign. US is the imaging tool of choice, with a sensitivity of more than 95%[30,31]. Since there is no consensus about the treatment of acute cholecystitis in pregnant women, more extensive data are needed. In the past, some Authors argued that in the absence of serious complications, conservative treatment could be preferred over operative management. The first consists in bowel rest, intravenous fluids, analgesic therapy and broad-spectrum antibiotics. Conversely, according to the most recent studies conservative approach is associated with higher relapse rates and foetal complications, and laparoscopic cholecystectomy is considered superior to non-operative management in the treatment of symptomatic cholecystitis[11,32,33].

Bowel obstruction. Small bowel obstruction (SBO) is extremely rare during pregnancy (nearly 0.001-0.003% of pregnancies). It is mainly caused by adhesions from previous abdominal surgery (70% of cases) and secondly by hernias, tumours, volvulus and intussusception[34]. Another significant cause of intestinal obstruction is previous major surgery for obesity (namely, the bariatric surgery), which has become widespread among young women of childbearing age, or endometriosis[35–37]; as a result, today the general surgeon has to face more frequently SBO in young pregnant women[38–40]. Clinical diagnosis results often difficult because symptoms are usually ascribed to the pregnant state. Urgent CT and MRI are commonly used to establish the correct diagnosis and to determine the aetiology of SBO[38–40].

Traditionally, it was advised to treat pregnant women conservatively avoiding surgery. Nevertheless, recent studies recommend the surgical intervention in case the initial conservative and supportive approach fails, taking into account that the overall rate of foetal loss is 17% and the maternal mortality rate is about 2%[41–43]. Laparotomy is usually performed by a midline incision to allow secure access to the coelomic cavity with a minimal handling of the uterus.(11)

Adnexal mass torsion. Adnexal torsion (AT) are not rare in non-pregnant state[44]. The most frequent cause of ovarian torsion or AT during pregnancy is represented by functional ovarian cysts, accounting for nearly 2.7% of emergent surgical interventions performed during pregnancy. Although the AT incidence during pregnancy is not defined, it is assumed to range between 0.2% and 22%, and it appears more frequent if ovulation has been pharmacologically induced[45–47]. AT can happen during every trimester, and early diagnostic and therapeutic laparoscopy is important in order to preserve maternal and foetal well-being. If a misdiagnosis occurs, AT can lead to ovarian necrosis up to sepsis with serious complications for the foetus, such as spontaneous abortion. Laparoscopic detorsion is usually a safe procedure also in

advanced gestational ages; ovariectomy instead is indicated if ovarian necrosis occurs.

PHYSIOLOGICAL CHANGES OF PREGNANCY: POTENTIAL PITFALLS FOR MISDIAGNOSIS

Pregnancy is characterized by many anatomical and physiological modifications that start to develop early in the first trimester. These changes can make difficult to recognize early signs of emergent conditions in pregnant women, who may have just blurred symptoms. This is the main reason explaining the common diagnostic delay of acute abdomen in pregnancy and the consequent delay of surgical intervention.

The plasma volume increases of about 50%, but this does not correspond to a simultaneous increase in the number of circulating blood cells, resulting in a pregnancy-induced anaemia. The increased plasmatic volume allows pregnant woman to face the significant blood loss that may occur during the delivery without any symptoms of shock, until late stages[48,49].

Since the utero-placental circulation has no autoregulation, pregnant women cardiac output increases to maintain blood pressure. This is made possible by the increased heart rate by 15-25% and the increased stroke volume by 20-30%. Central venous pressure and pulmonary capillary wedge pressure do not undergo any variations. During the course of the pregnancy, the gravid uterus is displaced cephalad and laterally so that it can cause aorto-caval compression and supine hypotensive syndrome, characterized by hypotension, tachycardia followed by bradycardia, sweating, pallor and nausea[50].

Moreover, a state of hypercoagulability is common during pregnancy, and this could lead to thromboembolic complications. Leukocyte count gradually rises (usually up to 12000-15000/mm3 and in some cases also up to 25000/mm3), but with no changes in immune capacity[51,52]. This leucocytosis can simulate an acute inflammatory process, or mask it.

With regard to respiratory system, progesterone levels induced by pregnancy determine an increase in tidal volume and an increase in oxygen consumption. The respiratory rate instead increases slightly (1–2 breaths/min), with an equivalent rise in alveolar ventilation. Consequently, a mild respiratory alkalosis not fully compensated by the reduction in serum bicarbonate is characteristic of the pregnant condition[53]. As a result of these physiological changes, a mild dyspnoea and a sense of breathlessness are commonly described by 70% of pregnant women from the beginning of the first trimester.

For what concern gastrointestinal (GI) physiology, progesterone decreases the enteric contractile activity and slow down intestinal transit resulting in constipation. Moreover, it decreases the tone of lower oesophageal sphincter (LES), resulting in the commonly experienced gastroesophageal reflux[54].

Another typical pregnancy-related sign is the rise of renal blood flow with the consequent increased glomerular filtration rate (GFR), that result in a decreased serum creatinine (the cut off for normality is 0.4–0.8 mg/dl). The dilatation of ureter and hydronephrosis occur frequently during pregnancy, due to hormonal changes and external compression by the gravid uterus[55].

All these physiological changes related to pregnancy allow to understand why the symptoms of non-obstetrical surgical pathologies in pregnant women are often confused with those characteristics of pregnancy. Moreover, too often the obstetrician does not have the global vision that would be useful to make a prompt diagnosis of a non-obstetrical problem. It is necessary to have the skills to understand when the problem is non-obstetric and referring to a surgeon with experience in surgical procedure during pregnancy. For that reason, moving the patient in a tertiary referral hospital with expertise about surgical procedures in pregnant women is suggested.

DIAGNOSTIC IMAGING DURING PREGNANCY

Radiological imaging during pregnancy represents a critical issue, that is currently still a source of debate. The main concern is the effect of ionizing radiation on the developing foetus, which can result in early pregnancy loss, foetal death, foetal growth retardation, microcephaly, malformations, central nervous system (CNS) defects and childhood tumours, especially leukaemia. It is important to consider that an embryo is more vulnerable to radiation during organogenesis (which occurs between 2 and 7 weeks after conception) and in the early foetal period (between 8 and 15 weeks after conception) compared to the following gestational ages[56–58].

Indeed, the period between 10 and 17 weeks of gestation is the most susceptible one for CNS teratogenesis[58].

The maximal cumulative radiation dose to the foetus, recommended by the mayor societies such as the National Council of Radiation Protection and Measurements and the American College of Radiology, should be less than 50-100 mGy during pregnancy[59,60]. More than 99% of foetuses exposed to radiation doses less than 20 mGy are healthy[61,62]. The American College of Obstetricians and Gynaecologists recognized that a ionizing radiation dose less than 5 rads has not been related with foetal complications, whereas a dose of 10-20 rads has been associated with foetal compromise[63,64] (**Table 2**).

Table 2
Foetal radiation dose and estimated threshold dose upon different gestational ages provided by different imaging procedures[58,63,69]

Diagnostic procedure	Foetal radiation dose (mGy)*	threshold
Chest X-ray	0.0005–0.01	
Abdominal X-ray	0.1–3.0	Early gestation (the first 2 weeks after conception) → 50-200 mGy
Chest CT or CT pulmonary angiography	0.01–0.66	Organogenesis (2–7 weeks after conception) → 200-250 mGy
Abdominal CT	1.3–35	
Pelvic CT	10-50	Early foetal period (8-15 weeks after conception) → 60–310 mGy
18F PET/CT whole-body scintigraphy	10-50	

*Foetal ionizing radiation exposure depends on gestational age, maternal body habitus and acquisition parameters.

On the other hand, if a pregnant woman is affected by an acute abdominal pain, the foetal outcome depends on the well-being of the mother and on the prompt diagnosis (that may necessitate of specific imaging techniques) and treatment.

The radiological diagnosis usually involves US, CT, and/or MRI. Women should be counselled before exposure to radiation and give their approval. Misperception about the safety of these procedures in pregnant women frequently causes a needless avoidance of advantageous imaging techniques. US and MRI are the imaging technique of choice during pregnancy because they are safe and are not associated with teratogenesis.

According to the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) guidelines, US is considered the first step in the diagnostic process[65]. It is considered safe and rapidly available. However, US is operator-dependent and can be easily limited by the patient habitus and the overlapping tissues. US sensitivity is up to 80%, whereas specificity reaches 94%. In 30% of patients with negative US imaging, other imagining techniques usually provide supplementary information[66].

Although CT scan is not the recommended first imaging technique during pregnancy, it has a key role when emergent situations occur, or after an abdominal trauma, or when a pregnant woman is affected by an acute abdominal pain and US scan do not provide diriment information, or when MRI is not available[67]. The iodinated contrast media can be administered because no mutagenic effects have been described after its use. The only potential harmful effect of iodinated contrast media within the foetus is represented by transitory thyroid function depression. For this reason, newborns screening for hypothyroidism is a good practice, and this check is even more fundamental in women who has received iodinated contrast medium during pregnancy[68].

Usually, pelvic CT radiation dose for the foetus is about 20 mGy but, since radiation exposure depends on the number of scan and adjacent image sections, it can reach nearly 50 mGy when a combined abdomen and pelvic scan is needed[65,69]. Nevertheless, in case of acute processes such as appendicitis or bowel obstruction during pregnancy, the maternal benefit from using such a radiological procedure may overcome the supposed foetal risk of ionizing radiation exposure.

Actually, MRI is considered a safer option respect to CT scan, since it provides high quality information without ionizing radiation exposure and can be performed at any gestational age. Therefore, when available, MRI should be preferred to CT scan in pregnant women with acute abdominal pain[70–72].

The US Food and Drug Administration stated that intravenous gadolinium is a class C agent having the capacity to cross the placenta. Although there are no sufficient data in literature to confirm whether gadolinium contrast has adverse consequences on the

foetus, its use during pregnancy should be avoided or performed only in selected cases when strictly essential for the health of the mother[68,73].

PERI-OPERATIVE MANAGEMENT AND ANAESTHESIA

Once the diagnosis of a non-obstetric disease in a pregnant woman is confirmed, and urgent surgical intervention turns out to be the most appropriate therapeutic approach, it is important to choose the most suitable surgical technique (laparotomy or laparoscopy) and correctly prepare the women to the surgery. A pregnant woman undergoing a surgical treatment should be evaluated preoperatively similarly to a non-pregnant patient.

In case of elective surgery, this should be deferred after delivery. Conversely, urgent surgical intervention should not be denied on the basis of gestational age, since accumulating evidence suggests that benefits of the surgery overcome the foetal risk. Although traditional recommendation suggests avoiding the first and third trimester to reduce the percentage of abortion and preterm labour, with most interventions performed during the second trimester[46], the most recent evidence does not confirmed them, recommending to perform surgery at any time during pregnancy when necessary and regardless of the gestational age[74,75].

During the time of intervention, it is essential for the obstetric care provider to be present in the institution, so that an emergent caesarean section could be done in case of maternal complications or foetal distress; moreover, neonatal and paediatric support should be rapidly accessible in the same health care centre.

Assumed the potential risk of some non-obstetric procedures for preterm labour and delivery, some Authors advocate the benefit of corticosteroid administration before intervention for foetuses at viable premature gestational ages[7].

Preoperative and postoperative foetal heart rate monitoring with cardiotocography is considered the current gold standard for urgent abdominal intervention after 24 weeks of gestation, with no need for intraoperative monitoring, because no foetal heart rate anomalies have been reported during surgical procedure[65,75,76]. In women before 24 weeks, confirmation of foetal well-being can be achieved with the US foetal heart beat in the immediate postoperative period.

Compared to the past, to date tocolysis is no longer used prophylactically before any type of surgery, but it is contemplated when threatened preterm labour is suspected. The specific tocolytic agent can be chosen independently on a case-by-case basis[77–79].

Since pregnancy determines a hypercoagulable state, prophylaxis for deep venous thrombosis is recommended in pregnant women undergoing surgical intervention. Moreover, insufflation of CO2 to induce pneumoperitoneum could even worsen the hypercoagulable state typical of the pregnant state, due to the venous stasis. Deep venous thrombosis prophylaxis implies the use of pneumatic compression devices and early postoperative mobilization. In addition, prophylactic administration of low molecular weight heparins may be recommended[19,80,81].

Regarding the intraoperative patient positioning, left lateral decubitus position appears the most appropriate in case of pregnant women undertaking surgery after the first trimester, with the aim to diminish aorto-caval compression induced by the gravid uterus[82,83].

Anaesthesia in a pregnant patient is another key point to be taken into account, since pregnancy determines changes in anaesthetic drugs metabolism and physical and mechanical modifications in women, which can complicate anaesthesiologist manoeuvres. The choice of the type of anaesthetic procedure should be guided by the type of intervention required; considering that today laparoscopy is usually preferred to open surgery, general anaesthesia is the most frequently applied technique[6]. The American Society of Anaesthesiologists (ASA) suggests that patients should be fasting from solid food for at least six hours prior to intervention; as for clear liquids, they should be avoided for over two hours prior to surgery.

Ventilation of the pregnant patient has an increased risk for aspiration and regurgitation and represents the most critical step in the anaesthesiologic process. The augmented oxygen consumption and the concomitant decreased functional residual capacity induced by the pregnant state, make the woman more susceptible to hypoxia caused by respiratory obstruction or difficult endotracheal intubation. To avoid this kind of complications, a rapid sequence intubation with cricoid pressure and a quickly acting muscle relaxant is suggested. It is necessary to maintain PCO2 levels balanced in the normal range for pregnancy; maternal hypercapnia can occur during deep anaesthesia and can determine the reduction

of uterine blood flow due to vasoconstriction, and consequently foetal acidosis. Instead, hypocapnia induced by excessive positive pressure ventilation influences maternal haemoglobin dissociation curve, with a reduction of oxygen release to the foetal tissues. Uterine vasoconstriction is also associated with uterine hyper tonus, that may further decrease uterine blood flow[84,85].

Although randomized clinical studies are not practicable in pregnant patients due to ethical reasons and most of our knowledge are based on animal models, most anaesthetic drugs have been demonstrated to be innocuous in the clinical practice. They show teratogenic effects only when administered at high doses or directly to the foetus. Local and volatile anaesthetics, induction drugs, neuromuscular blocking agents and opioids can be securely used at standard dosages when the normal physiology of pregnancy is maintained[86,87].

Besides, it is important to emphasize that pregnancy is characterized by an increased sensitivity to volatile anaesthetic drugs; for example, in animal studies the need for halogenated agents has been demonstrated to be decreased up to 40% by the second trimester[86,87].

SURGICAL TECHNIQUES

When a pregnant woman requires a surgical intervention for non-obstetric reasons, whether to perform a laparoscopy or an open surgery is often debated. Historically, laparotomy was considered the technique of choice, since surgeons were used to practice open intervention instead of laparoscopy, which was considered contraindicated for the potential risk of gravid uterus damage from Veress or trocars insertion. Laparoscopy was thought to be hard to perform for the mechanical presence of the enlarged uterus, the risk of foetal hypoxia and acidaemia, and the maternal risk of decreased venous blood return secondary to induction of pneumoperitoneum[88,89].

Currently, laparotomy is still reserved for pregnant women with small bowel intestinal obstruction (SBO), especially due to adhesions from previous surgery or preceding bariatric surgery, after the failure of the conservative management[38,42,90]. Also in case of tumours diagnosed during pregnancy[91], such as vulvar carcinoma, ovarian tumour, and cervical cancer, laparotomy appears to be the most appropriate surgical technique when surgery is required. In these cases, treatment needs to be individualized, and if definitive radical surgery is needed, it should not be delayed after the delivery[92–95].

Recently, many studies and case reports have demonstrated the safety of performing laparoscopic surgery during pregnancy, which has become a standard procedure. In case of appendicitis, cholecystitis and adnexal mass complications, laparoscopy can be safely performed and, according to recent data, seems even superior to open surgery[65,75,96–99]. Laparoscopic appendicectomy is the most common procedure performed during pregnancy[100,101]. Complex surgical procedures, like adrenalectomy, nephrectomy and splenectomy, can also be achieved laparoscopically in pregnant women[102–105]. Laparoscopic surgery results safe, feasible, and effective during pregnancy; foetal outcomes are more likely to be unfavourably affected by the underlying disease and misdiagnosis rather than the procedure itself[106].

Compared to open surgery, laparoscopy has many advantages[107–109], like shorter operative times, reduced length of hospital stays, fewer surgical complications, less postoperative wound infection and ileus, less postoperative pain and earlier return to normal activity and mobility, which is crucial in preventing thromboembolism[110], even in pregnancy[46,111–114]. Some data suggested that open surgery rather than laparoscopy seems to have an increased risk for obstetric and foetal complications, such as preterm labour, preterm delivery, and abortion[29]. Conversely, other studies show, for example, that laparoscopic appendicectomy has higher rates of foetal loss rather than open appendicectomy[106,115,116]. Therefore, other studies are needed to make stronger recommendations.

With regard to the surgical laparoscopic technique, the primary abdominal access can be carefully accomplished by skilled surgeons with an open procedure (Hasson technique), a Veress needle, or an optical trocar technique[117]. As for Veress needle, instead of using the default periumbilical site of insertion, it can be positioned in alternative and safer points, based on the gestational age. One of this substitute points is the Palmer's point, sited in the upper left quadrant, which is the second most common insertion site used in laparoscopy. Another different point is named Latif's point, that is sited in the right angle between the xiphoid process and the right costal margin. Instead, the Lee-Huang's point is the midpoint between the umbilicus and xiphoid process. All these alternative points can be used as other site of Veress insertion or otherwise for trocars or camera site insertion, especially in

pregnant patients[12,118–122].

Comparing to Veress needle procedure, the Hasson open technique is easier to perform, with no difference in surgical time, and it avoids the possibility to cause pneumoamnion, which determines fatal consequences for the fetus[123].

Therefore, changing the site of initial abdominal access on the basis of uterine fundal height, using both Veress and Hasson techniques, has been demonstrated to be safe and effective during pregnancy and central to avoid potential injury to the uterus or other intra-abdominal organs.

In order to avoid other complications of laparoscopic procedure in pregnant patient, such as potential foetal acidosis and foetal instability induced by CO2 insufflation, it is important to maintain pneumoperitoneum pressure stable at values of about 10-15 mmHg, which have been demonstrated to be safe and without complications both for the mother and the foetus[33,65,106].

CONCLUSIONS

Non-obstetric surgery in pregnant patients has been proved to be safe if performed by a highly specialized team composed by skilled surgeons and obstetricians. When a pregnant woman suffers from an acute abdominal pain, whose non-obstetric origin has been demonstrated, conservative management may adversely affect pregnancy outcomes and foetal well-being. For this reason, a surgical intervention should not be deferred only because of the gravid status of the patient.

In the past years, limited evidences from mainly case reports and retrospective studies demonstrated that both laparotomic and laparoscopic techniques can be applied during pregnancy without maternal or foetal consequences, particularly when physiological and anatomical changes of pregnancy are considered, and appropriate adjustments are made by the anaesthesiologist.

Even if surgical procedures in pregnancy are performed with increasing frequency to date, the use of laparoscopy in pregnant women is still not widespread and not practiced by many surgeons. Moreover, complications of laparoscopy are often not mentioned or analysed in these small series and studies. Consequently, in many hospital settings there is still a lack of knowledge and many surgeons are reluctant to practice surgery in pregnant patients, especially laparoscopy.

However, the few recent available data support non-obstetric surgery's safety and efficacy when performed by a skilled, multidisciplinary equip. Nevertheless, more data and are still needed to make strong recommendations and guidelines.

REFERENCES

1) Casarin J, Laganà AS, Uccella S, Cromi A, Pinelli C, Gisone B, et al. **Surgical treatment of large adnexal masses: a retrospective analysis of 330 consecutive cases.** Minimally Invasive Therapy & Allied Technologies, 2019:1–9.

2) Garzon S, Laganà AS, Pomini P, Raffaelli R, Ghezzi F, Franchi M. **Laparoscopic reversible occlusion of uterine arteries and cornuostomy for advanced interstitial pregnancy.** Minimally invasive therapy & allied technologies, 2018; 4:1–4.

3) Franchi M, Uccella S, Zorzato PC, Dalle Carbonare A, Garzon S, Laganà AS, et al. **Vaginal flap for urethral neomeatus reconstruction after radical surgery for vulvar cancer: a retrospective cohort analysis.** International Journal of Gynecological Cancer, 2019; 0:1–7.

4) Baggio S, Laganà AS, Garzon S, Scollo M, Raffaelli R, Tateo S, et al. **Efficacy of a collagen-fibrin sealant patch (TachoSil®) as adjuvant treatment in the inguinofemoral lymphadenectomy for vulvar cancer: a double-blind randomized-controlled trial**. Archives of Gynecology and Obstetrics, 2019.

5) National Institute for Health Research. **General surgery is mostly safe during pregnancy**. 2017.

6) Nejdlova M, Johnson T. **Anaesthesia for non-obstetric procedures during pregnancy.** Continuing Education in Anaesthesia Critical Care & Pain, 2012; 12(4):203–206.

7) The American College of Obstetricians and Gynecologist. ACOG committe opinion No 775. **Nonobstetric surgery during pregnancy**. Obstetrics & Gynecology, 2019; 133(4).

8) Balinskaite V, Bottle A, Sodhi V, Rivers A, Bennett PR, Brett SJ, et al. **The Risk of Adverse Pregnancy Outcomes Following Nonobstetric Surgery During Pregnancy: Estimates From a Retrospective Cohort Study of 6.5 Million Pregnancies**. Annals of Surgery, 2017; 266(2):260–266.

9) Barakat RMB, Garzon S, Laganà AS, Franchi M, Ghezzi F. **Fetus-in-fetu: a rare condition that requires common rules for its definition**. Archives of Gynecology and Obstetrics, 2019.

10) Franchi M, Raffaelli R, Baggio S, Scollo M, Garzon S,

Laganà AS, et al. **Unintentional transvesical caesarean section: incidence, risk factors, surgical technique and post-operative management**. European Journal of Obstetrics, Gynecology, and Reproductive Biology, 2019; 236:26–31.
11) Zachariah SK, Fenn M, Jacob K, Arthungal SA, Zachariah SA. **Management of acute abdomen in pregnancy: current perspectives**. International Journal of Women's Health, 2019; Volume 11:119–134.
12) Malangoni MA. **Gastrointestinal surgery and pregnancy**. Gastroenterology Clinics of North America, 2003; 32(1):181–200.
13) Augustin G, Majerovic M. **Non-obstetrical acute abdomen during pregnancy.** European Journal of Obstetrics & Gynecology and Reproductive Biology, 2007; 131(1):4–12.
14) Skubic JJ, Salim A. **Emergency general surgery in pregnancy.** Trauma Surgery & Acute Care Open, 2017; 2(1):e000125.
15) Yilmaz HG, Akgun Y, Bac B, Celik Y. **Acute appendicitis in pregnancy — risk factors associated with principal outcomes: A case control study**. International Journal of Surgery, 2007; 5(3):192–197.
16) Choi JJ, Mustafa R, Lynn ET, Divino CM. **Appendectomy During Pregnancy: Follow-Up of Progeny**. Journal of the American College of Surgeons, 2011; 213(5):627–632.
17) Ueberrueck T, Koch A, Meyer L, Hinkel M, Gastinger I. **Ninety-four Appendectomies for Suspected Acute Appendicitis during Pregnancy**. World Journal of Surgery, 2004; 28(5):508–511.
18) Hodjati H, Kazerooni T. **Location of the appendix in the gravid patient: a re-evaluation of the established concept.** International Journal of Gynecology & Obstetrics, 2003; 81(3):245–247.
19) Melnick DM, Wahl WL, Dalton VK. **Management of general surgical problems in the pregnant patient.** The American Journal of Surgery, 2004; 187(2):170–180.
20) Popkin CA, Lopez PP, Cohn SM, Brown M, Lynn M. **The incision of choice for pregnant women with appendicitis is through McBurney's point.** The American Journal of Surgery, 2002; 183(1):20–22.
21) Baer JL, Reis RA, Arens RA. **Appendicitis in pregnancy: with changes in position and axis of the normal appendix in pregnancy**. JAMA, 1932; 98(16):1359–1364.
22) Ishaq A, Khan MJ, Pishori T, Soomro R, Khan S. **Location of appendix in pregnancy: does it change?** Clinical and Experimental Gastroenterology, 2018; 11:281–287.
23) Williams R, Shaw J. **Ultrasound scanning in the diagnosis of acute appendicitis in pregnancy.** Emergency Medicine Journal, 2007; 24(5):359–360.
24) Rosen MP, Ding A, Blake MA, Baker ME, Cash BD, Fidler JL, et al. **ACR Appropriateness Criteria® Right Lower Quadrant Pain—Suspected Appendicitis.** Elsevier Journal of the American College of Radiology, 2011; 1(11):749–755.
25) Mervak BM, Wilson SB, Handly BD, Altun E, Burke LM. **MRI of acute appendicitis**. Journal of Magnetic Resonance Imaging, 2019.
26) Ellington SR, Flowers L, Legardy-Williams JK, Jamieson DJ, Kourtis AP. **Recent trends in hepatic diseases during pregnancy in the United States, 2002–2010**. American Journal of Obstetrics and Gynecology, 2015; 212(4):524.e1-524.e7.
27) Date RS, Kaushal M, Ramesh A. **A review of the management of gallstone disease and its complications in pregnancy.** The American Journal of Surgery, 2008; 196(4):599–608.
28) Ko CW, Beresford SAA, Schulte SJ, Matsumoto AM, Lee SP. **Incidence, natural history, and risk factors for biliary sludge and stones during pregnancy.** Hepatology, 2005; 41(2):359–365.
29) Sachs A, Guglielminotti J, Miller R, Landau R, Smiley R, Li G. **Risk Factors and Risk Stratification for Adverse Obstetrical Outcomes After Appendectomy or Cholecystectomy During Pregnancy.** JAMA Surgery, 2017; 152(5):436.
30) Dietrich CS, Hill CC, Hueman M. **Surgical Diseases Presenting in Pregnancy.** Surgical Clinics of North America, 2008; 88(2):403–419.
31) Borzellino G, Motton MA, Minniti F, Montemezzi S, Tomezzoli A, Genna M. **Sonographic diagnosis of acute cholecystitis in patients with symptomatic gallstones: Sonographic Diagnosis of Acute Cholecystitis in Patients.** Journal of Clinical Ultrasound, 2016; 44(3):152–158.
32) Jelin EB, Smink DS, Vernon AH, Brooks DC. **Management of biliary tract disease during pregnancy: a decision analysis.** Surgical Endoscopy, 2008; 22(1):54–60.
33) Juhasz-Böss I, Solomayer E, Strik M, Raspé C. **Abdominal Surgery in Pregnancy**. Deutsches Aerzteblatt Online, 2014.
34) Sivanesaratnam V. **The acute abdomen and the obstetrician**. Best Practice & Research: Clinical Obstetrics & Gynaecology, 2000; 14(1):89–102.
35) Raffaelli R, Garzon S, Baggio S, Genna M, Pomini P, Laganà AS, et al. **Mesenteric vascular and nerve sparing surgery in laparoscopic segmental intestinal resection for deep infiltrating endometriosis.** European Journal of Obstetrics, Gynecology, and Reproductive Biology, 2018; 231:214–219.
36) Laganà AS, Vitale SG, Trovato MA, Palmara VI, Rapisarda AMC, Granese R, et al. **Full-Thickness Excision versus Shaving by Laparoscopy for Intestinal Deep Infiltrating Endometriosis: Rationale and Potential Treatment Options.** BioMed Research International, 2016; 2016:3617179.
37) Barra F, Laganà AS, Casarin J, Ghezzi F, Ferro Desideri L, Scala C, et al. **Molecular Targets for Endometriosis Therapy: Where We Are and Where We Are Going?** International Journal of Fertility & Sterility, 2019; 13(2):89–92.
38) Vannevel V, Jans G, Bialecka M, Lannoo M, Devlieger R, Van Mieghem T. **Internal Herniation in Pregnancy After Gastric Bypass: A Systematic Review.** Obstetrics & Gynecology, 2016; 127(6):1013–1020.
39) Katawala T, Hamlyn EL. **Complete small bowel obstruction secondary to transomental herniation in pregnancy.** International Journal of Surgery Case

Reports, 2011; 2(4):51–52.
40) Royal College of Obstetricians and Gynaecologist. **Care of Women with Obesity in Pregnancy.** Green-top Guidelines No.72. BJOG: An International Journal of Obstetrics & Gynaecology, 2018.
41) Latha Maheswari S, Abraham Reena, Chitra TV. **Intestinal obstruction in pregnancy: three case reports.** International Journal of Reproduction, Contraception, Obstetrics and Gynecology, 2013:491–493.
42) Webster P, Bailey M, Wilson J, Burke D. **Small bowel obstruction in pregnancy is a complex surgical problem with a high risk of fetal loss.** The Annals of The Royal College of Surgeons of England, 2015; 97(5):339–344.
43) Sagi Y, Bussiere-Cote S, Meier K, Bischoff D, D'Souza R. **Small Bowel Obstruction in Pregnancy: A Systematic Review.** Obstetrics & Gynecology, 2018; 131.
44) Laganà AS, Sofo V, Salmeri FM, Palmara VI, Triolo O, Terzić MM, et al. **Oxidative Stress during Ovarian Torsion in Pediatric and Adolescent Patients: Changing The Perspective of The Disease.** International Journal of Fertility & Sterility, 2016; 9(4):416–423.
45) Daykan Y, Bogin R, Sharvit M, Klein Z, Josephy D, Pomeranz M, et al. **Adnexal Torsion during Pregnancy: Outcomes after Surgical Intervention—A Retrospective Case-Control Study.** Journal of Minimally Invasive Gynecology, 2019; 26(1):117–121.
46) Fatum M, Rojansky N. **Laparoscopic Surgery During Pregnancy.** Obstetrical and Gynecological Survey, 2001:10.
47) Asfour V, Varma R, Menon P. **Clinical risk factors for ovarian torsion.** Journal of Obstetrics and Gynaecology, 2015; 35(7):721–725.
48) Bhatia P, Chhabra S. **Physiological and anatomical changes of pregnancy: Implications for anaesthesia.** Indian Journal of Anaesthesia, 2018; 62(9):651–657.
49) Chandra S, Tripathi AK, Mishra S, Amzarul M, Vaish AK. **Physiological Changes in Hematological Parameters During Pregnancy.** Indian Journal of Hematology and Blood Transfusion, 2012; 28(3):144–146.
50) Lanni SM, Tillinghast J, Silver HM. **Hemodynamic changes and baroreflex gain in the supine hypotensive syndrome.** American Journal of Obstetrics and Gynecology, 2002; 187(6):1636–1641.
51) Stirrat GM. **Pregnancy and immunity.** British Medical Journal, 1994; 308.
52) Yeomans ER, Gilstrap LC. **Physiologic changes in pregnancy and their impact on critical care**: Critical Care Medicine, 2005; 33(Supplement):S256–S258.
53) LoMauro A, Aliverti A. **Respiratory physiology of pregnancy.** Breathe, 2015; 11(4):297–301.
54) Whitehead EM, Smith M, Dean Y, O'Sullivan G. **An evaluation of gastric emptying times in pregnancy and the puerperium.** Anaesthesia, 1993; 48(1):53–57.
55) Cheung KL, Lafayette RA. **Renal Physiology of Pregnancy- ClinicalKey.** Advances in Chronic Kidney Disease, 2013; 20(3):209-14.
56) International Commission on Radiological Protection. **Pregnancy and medical radiation.** Annals of the ICRP, 2000; 30(1):iii–viii, 1–43.
57) Williams PM, Col L. **Health Effects of Prenatal Radiation Exposure**. 2010; 82(5):6.
58) Groen RS, Bae JY, Lim KJ. **Fear of the unknown: ionizing radiation exposure during pregnancy.** American Journal of Obstetrics and Gynecology, 2012; 206(6):456–462.
59) National Council on Radiation Protection and Measurements. **Medical radiation exposure of pregnant and potentially pregnant women.** NCRP report no 54. Bethesda, MD: National Council on Radiation Protection and Measurements, 1977.
60) Andreotti RF, Lee SI, Choy G, DeJesus AS, Bennett GL, Brown DL, et al. **ACR Appropriateness Criteria on acute pelvic pain in the reproductive age group.** J Am Coll Radiol., 2009; 6(4):235–41.
61) Goldberg-Stein SA, Liu B, Hahn PF, Lee SI. **Radiation Dose Management: Part 2, Estimating Fetal Radiation Risk From CT During Pregnancy.** American Journal of Roentgenology, 2012; 198(4):W352–W356.
62) Gomes M, Matias A, Macedo F. **Risks to the fetus from diagnostic imaging during pregnancy: review and proposal of a clinical protocol.** Pediatric Radiology, 2015; 45(13):1916–1929.
63) The American College of Obstetricians and Gynecologist. ACOG committe opinion No. 723. **Guidelines for Diagnostic Imaging During Pregnancy and Lactation.** Obstetrics & Gynecology, 2017; 130(4).
64) Santis MD, Cesari E, Nobili E, Straface G, Cavaliere AF, Caruso A. **Radiation effects on development.** Birth Defects Research Part C: Embryo Today: Reviews, 2007; 81(3):177–182.
65) Pearl JP, Price RR, Tonkin AE, Richardson WS, Stefanidis D. **SAGES guidelines for the use of laparoscopy during pregnancy.** Surgical Endoscopy, 2017; 31(10):3767–3782.
66) Masselli G, Brunelli R, Monti R, Guida M, Laghi F, Casciani E, et al. **Imaging for acute pelvic pain in pregnancy.** Insights into Imaging, 2014; 5(2):165–181.
67) Katz DS, Khalid M, Coronel EE, Mazzie JP. **Computed Tomography Imaging of the Acute Pelvis in Females.** Canadian Association of Radiologists Journal, 2013; 64(2):108–118.
68) Webb JAW, Thomsen HS, Morcos SK, Members of Contrast Media Safety Committee of European Society of Urogenital Radiology (ESUR). **The use of iodinated and gadolinium contrast media during pregnancy and lactation.** European Radiology, 2005; 15(6):1234–1240.
69) Tremblay E, Thérasse E, Thomassin-Naggara I, Trop I. **Quality Initiatives: Guidelines for Use of Medical Imaging during Pregnancy and Lactation.** RadioGraphics, 2012; 32(3):897–911.
70) Masselli G, Derme M, Laghi F, Framarino-dei-Malatesta M, Gualdi G. **Evaluating the Acute Abdomen in the Pregnant Patient.** Radiologic Clinics of North America, 2015; 53(6):1309–1325.
71) Lubarsky M, Kalb B, Sharma P, Keim SM, Martin DR. **MR Imaging for Acute Nontraumatic Abdominopelvic Pain: Rationale and Practical Considerations.** RadioGraphics, 2013; 33(2):313–337.
72) Kanal E, Barkovich AJ, Bell C, Borgstede JP, Bradley WG, Froelich JW, et al. **ACR guidance document on MR safe practices: 2013.** Journal of Magnetic Resonance

Imaging, 2013; 37(3):501–530.
73) Garcia-Bournissen F, Shrim A, Koren G. **Safety of gadolinium during pregnancy. 2006.**
74) Weiner E, Mizrachi Y, Keidar R, Kerner R, Golan A, Sagiv R. **Laparoscopic surgery performed in advanced pregnancy compared to early pregnancy.** Archives of Gynecology and Obstetrics, 2015; 292(5):1063–1068.
75) Rollins MD, Chan KJ, Price RR. **Laparoscopy for appendicitis and cholelithiasis during pregnancy: a new standard of care.** Surgical Endoscopy, 2004; 18(2):237–241.
76) Weissmann-Brenner A, Haiman S, Ayala MM, Gindes L, Achiron R, Sivan E, et al. **Maternal medical compromise during pregnancy and pregnancy outcomes.** The Journal of Maternal-Fetal & Neonatal Medicine, 2015; 28(10):1202–1207.
77) Illanes SE, Pérez-Sepúlveda A, Rice GE, Mitchell MD. **Preterm labour: association between labour physiology, tocolysis and prevention.** Expert Opinion on Investigational Drugs, 2014; 23(6):759–771.
78) Katz VL, Farmer RM. **Controversies in tocolytic therapy.** Clinical Obstetrics and Gynecology, 1999; 42(4):802–819.
79) Romero R, Sibai BM, Sanchez-Ramos L, Valenzuela GJ, Veille J-C, Tabor B, et al. **An oxytocin receptor antagonist (atosiban) in the treatment of preterm labor: A randomized, double-blind, placebo-controlled trial with tocolytic rescue.** American Journal of Obstetrics and Gynecology, 2000; 182(5):1173–1183.
80) Jorgensen JO, Lalak NJ, North L, Hanel K, Hunt DR, Morris DL. **Venous stasis during laparoscopic cholecystectomy.** Surgical Laparoscopy & Endoscopy, 1994; 4(2):128–133.
81) Casele HL. **The Use of Unfractionated Heparin and Low Molecular Weight Heparins in Pregnancy.** Clinical Obstetrics and Gynecology, 2006; 49(4):895.
82) Sanghavi M, Rutherford JD. **Cardiovascular Physiology of Pregnancy.** Circulation, 2014; 130(12):1003–1008.
83) Fujitani S, Baldisseri MR. **Hemodynamic assessment in a pregnant and peripartum patient: Critical Care Medicine**, 2005; 33(Supplement):S354–S361.
84) Fanzago E. **Anaesthesia for non obstetric surgery in pregnant patients.** Minerva Anestesiologica, 2003; 69(5):12.
85) Goodman S. **Anesthesia for nonobstetric surgery in the pregnant patient.** Seminars in Perinatology, 2002; 26(2):136–145.
86) Kuczkowski KM. **The safety of anaesthetics in pregnant women.** Expert Opinion on Drug Safety, 2006; 5(2):251–264.
87) Reitman E, Flood P. **Anaesthetic considerations for non-obstetric surgery during pregnancy.** British Journal of Anaesthesia, 2011; 107:i72–i78.
88) Kilpatrick CC, Orejuela FJ. **Management of the acute abdomen in pregnancy: a review**: Current Opinion in Obstetrics and Gynecology, 2008; 20(6):534–539.
89) Saunders P, Milton PJD. **Laparotomy during Pregnancy: An Assessment of Diagnostic Accuracy and Fetal Wastage.** British Medical Journal, 1973; 3:165–167.
90) Staszewicz W, Christodoulou M, Marty F, Bettschart V. **Damage control surgery by keeping the abdomen open during pregnancy: favorable outcome, a case report.** World Journal of Emergency Surgery, 2009; 4(1):33.
91) Sartori E, Franchi M, Capelli G, Cicinelli E, Colacurci N, Vincenzo RD, Landoni F, Maggino T, Masturzo B, Parazzini F, Scarfone G, Peccatori F, Romagnolo C, Scibilia G, Scollo P, et al. **Cancer in pregnancy: proposal of an Italian multicenter study. Gynecologic Oncology Group of the Italian Society of Gynecology and Obstetrics (SIGO).** Italian Journal of Gynæcology & Obstetrics, 2018; (3):37–44.
92) Sivanesaratnam V, Pathmanathan R. **Carcinoma of the vulva in pregnancy: a rare occurrence.** Asia-Oceania Journal of Obstetrics and Gynaecology, 1990; 16(3):207–210.
93) Ogunleye D, Lewin SN, Huettner P, Herzog TJ. **Recurrent vulvar carcinoma in pregnancy.** Gynecologic Oncology, 2004; 95(2):400–401.
94) Han SN, Mhallem Gziri M, Van Calsteren K, Amant F. **Cervical cancer in pregnant women: treat, wait or interrupt? Assessment of current clinical guidelines, innovations and controversies.** Therapeutic Advances in Medical Oncology, 2013; 5(4):211–219.
95) Panayotidis C, Lim M, Martin JE. **Laparoscopy versus laparotomy for the treatment of ovarian cysts in pregnancy: should we change our conventional way of practice?** Gynecological Surgery, 2005; 2(2):83–87.
96) Arafat M, Ghaffar I, El-Hussainy A, Abd Alkhalik M, Ahmad M, Mostafa T. **Safety and feasibility of laparoscopic cholecystectomy during pregnancy.** Journal of The Arab Society for Medical Research, 2016; 11(1):9.
97) Nasioudis D, Tsilimigras D, Economopoulos KP. **Laparoscopic cholecystectomy during pregnancy: A systematic review of 590 patients.** International Journal of Surgery, 2016; 27:165–175.
98) Cox TC, Huntington CR, Blair LJ, Prasad T, Lincourt AE, Augenstein VA, Heniford BT. **Laparoscopic appendectomy and cholecystectomy versus open: a study in 1999 pregnant patients.** Surgical Endoscopy, 2016; 30(2):593–602.
99) Ye P, Zhao N, Shu J, Shen H, Wang Y, Chen L, Yan X. **Laparoscopy versus open surgery for adnexal masses in pregnancy: a meta-analytic review.** Archives of Gynecology and Obstetrics, 2019; 299(3):625–634.
100) Chakraborty J, Kong JC, Su WK, Gourlas P, Gillespie C, Slack T, Morris B, Lutton N. **Safety of laparoscopic appendicectomy during pregnancy: a systematic review and meta-analysis: Laparoscopic appendicectomy during pregnancy.** ANZ Journal of Surgery, 2019.
101) Wilasrusmee C, Sukrat B, McEvoy M, Attia J, Thakkinstian A. **Systematic review and meta-analysis of safety of laparoscopic versus open appendicectomy for suspected appendicitis in pregnancy.** British Journal of Surgery, 2012; 99(11):1470–1478.
102) Lee D, Abraham N. **Laparoscopic radical nephrectomy during pregnancy: case report and review of the literature.** Journal of Endourology, 2008;

22(3).
103) Felbinger TW, Posner M, Eltzschig HK, Kodali BS. **Laparoscopic splenectomy in a pregnant patient with immune thrombocytopenic purpura.** International Journal of Obstetric Anesthesia, 2007; 16(3):281–283.
104) Mahey R, Kaur SD, Chumber S, Kriplani A, Bhatla N. **Splenectomy during pregnancy: treatment of refractory immune thrombocytopenic purpura.** BMJ Case Reports, 2013; 2013.
105) Arvind NK, Singh O, Gupta SS, Sahay S, Ali K, Dharaskar A. **Laparoscopic Nephrectomy for Pyonephrosis During Pregnancy: Case Report and Review of the Literature.** Reviews in Urology, 2011; 13(2):98–103.
106) Lee SH, Lee JY, Choi YY, Lee JG. **Laparoscopic appendectomy versus open appendectomy for suspected appendicitis during pregnancy: a systematic review and updated meta-analysis.** BMC Surgery, 2019; 19(1).
107) Lagana AS, Vitale SG, De Dominici R, Padula F, Rapisarda AMC, Biondi A, Cianci S, Valenti G, Capriglione S, Frangez HB, Sturlese E. **Fertility outcome after laparoscopic salpingostomy or salpingectomy for tubal ectopic pregnancy A 12-years retrospective cohort study.** Annali Italiani Di Chirurgia, 2016; 87:461–465.
108) Garzon S, Raffaelli R, Montin U, Ghezzi F. **Primary hepatic pregnancy: report of a case treated with laparoscopic approach and review of the literature.** Fertility and Sterility, 2018; 110(5):925-931.e1.
109) Laganà AS, Santoro G, Triolo O, Giacobbe V, Certo R, Palmara V. **Hashimoto thyroiditis onset after laparoscopic removal of struma ovarii: an overview to unravel a rare and intriguing finding.** Clinical and Experimental Obstetrics & Gynecology, 2015; 42(5):673–678.
110) Sturlese E, Triolo O, Grasso R, Laganà AS, Retto A, Rossetti D, Vitale SG, Sarpietro G, De Dominici R. **Thromboembolism prophylaxis in laparoscopic surgery for gynecologic benign diseases. Results of a single center experience in 922 procedures.** Annali Italiani Di Chirurgia, 2017; 88:342–347.
111) Erekson EA, Brousseau EC, Dick-Biascoechea MA, Ciarleglio MM, Lockwood CJ, Pettker CM. **Maternal postoperative complications after nonobstetric antenatal surgery.** The Journal of Maternal-Fetal & Neonatal Medicine, 2012; 25(12):2639–2644.
112) Conron RW, Abbruzzi K, Cochrane SO, Sarno AJ, Cochrane PJ. **Laparoscopic procedures in pregnancy.** The American Surgeon, 1999; 65(3):259–263.
113) Lyass S, Pikarsky A, Eisenberg VH, Elchalal U, Schenker JG, Reissman P. **Is laparoscopic appendectomy safe in pregnant women?** Surgical Endoscopy, 2001; 15(4):377–379.
114) Rojansky N, Shushan A, Fatum M. **Laparoscopy versus laparotomy in pregnancy: a comparative study.** The Journal of the American Association of Gynecologic Laparoscopists, 2002; 9(1):108–110.
115) Walker HGM, Al Samaraee A, Mills SJ, Kalbassi MR. **Laparoscopic appendicectomy in pregnancy: A systematic review of the published evidence.** International Journal of Surgery, 2014; 12(11):1235–1241.
116) Winter NN, Guest GD, Bozin M, Thomson BN, Mann GB, Tan SBM, Clark DA, Daruwalla J, Muralidharan V, Najan N, Pitcher ME, Vilhelm K, Cox MR, Lane SE, Watters DA. **Laparoscopic or open appendicectomy for suspected appendicitis in pregnancy and evaluation of foetal outcome in Australia.** ANZ journal of surgery, 2017; 87(5):334–338.
117) Vitale SG, Gasbarro N, Lagana AS, Sapia F, Rapisarda AMC, Valenti G, Trovato MA, Rossetti D, Chiofalo B, Barrasso G, Tinelli A, Corrado F. **Safe introduction of ancillary trocars in gynecological surgery: the "yellow island" anatomical landmark.** Annali Italiani Di Chirurgia, 2016; 87:608–611.
118) Upadhyay A, Stanten S, Kazantsev G, Horoupian R, Stanten A. **Laparoscopic management of a nonobstetric emergency in the third trimester of pregnancy.** Surgical Endoscopy, 2007; 21(8):1344–1348.
119) Abd Ellatif ME, Ghnnam WM, Abbas A, Basheer M, Dawoud I, Ellaithy R. **Latif's point: A new point for Veress needle insertion for pneumoperitoneum in difficult laparoscopy: Latif's new access point.** Asian Journal of Endoscopic Surgery, 2018; 11(2):133–137.
120) Huang KG, Chua AA, Lee CL. **Surgical Trocar Insertion Among Pregnant Patients.** International Journal of Gynecological Cancer, 2014; 24(6).
121) Wang C-J, Yen C-F, Lee C-L, Soong Y-K. **Minilaparoscopic Cystectomy and Appendectomy in Late Second Trimester**. 2002:3.
122) Correa-Paris A, Suárez-Salvador E, Gomar Crespo A, Puig Puig O, Xercavins J, Gil-Moreno A. **Closed entry technique for the laparoscopic management of adnexal mass during pregnancy.** Gynecological Surgery, 2014; 11(3):213–218.
123) Friedman JD, Ramsey PS, Ramin KD, Berry C. **Pneumoamnion and Pregnancy Loss After Second-Trimester Laparoscopic Surgery.** The American College of Obstetricians and Gynecologists, 2002; 99(3).
124) Casey BM and Cox, SM. **Cholecystitis in pregnancy.** Infectious Diseases in Obstetrics and Gynecology, 1996; 4:303–309.
125) Mendez-Figueroa H, Dahlke JD, Vrees RA, Rouse DJ. **Trauma in pregnancy: an updated systematic review.** American Journal of Obstetrics and Gynecology, 2013; 209(1):1–10.
126) Hill CC, Pickinpaugh J. **Trauma and Surgical Emergencies in the Obstetric Patient.** Surgical Clinics of North America, 2008; 88(2):421–440.