CERVICAL CANCER DURING PREGNANCY. DIAGNOSTIC AND TREATMENT OPTIONS.

I. Goidescu*,,# Ioana C. Rotar*,***,#, F. Stamatian*,**,***, D. Mureşan*,**,***

* *University of Medicine and Pharmacy „Iuliu Haţieganu" Cluj Napoca*
** *IMOGEN Research Center Institute*
*** *Clinical County Emergency Hospital, Cluj-Napoca*

Abstract

Cervical cancer is the most common malignancy diagnosed during pregnancy and the psycho-emotional impact created by this pathology is important.

Treatment of cervical cancer during pregnancy should be conducted by a multidisciplinary team that can advise the couple regarding the best treatment options taking into account the gestational age and the couple's desire to keep the pregnancy or to maintain the reproductive function.

Our article aims to review the main diagnostic methods and therapeutic conduct, especially in the early forms of cervical cancer diagnosed in pregnancy.

Rezumat: Cancerul cervical în sarcină. Diagnostic şi conduită terapeutică.

Cancerul de col este cea mai frecventă neoplazie diagnosticată în sarcină, iar impactul psiho-emoţional creat de această patologie este unul important.

Tratamentul cancerului de col în sarcină trebuie să fie realizat de o echipă multidisciplinară care să poată prezenta cuplului cele mai bune opţiuni de tratament raportate bineînţeles la vârsta gestaţională şi la dorinţa cuplului de a păstra sarcina sau de a avea şi alţi copii.

Articolul nostru îţi propune să treacă în revistă principalele metode diagnostice precum şi conduita terapeutică, mai ales în formele incipiente de cancer cervical diagnosticat în sarcină.

Cuvinte cheie: cancer de col, colposcopie, sarcină, neoplazie intraepitelială cervicală

 # - Iulian Goidescu and Ioana Rotar have equally contributed to this work

Introduction

Gynecologic cancers are among the most common malignancies diagnosed during pregnancy; and cervical location representing around 70% of these malignancies **[1, 2]**. The incidence of cervical cancer in pregnancy ranges from 1/ 1200-10000 pregnancies **[3, 4].** The trend of delaying childbearing after 30 years in developed countries is associated with an increased incidence of cervical cancer detection in pregnancy **[3, 4]**.

Most women diagnosed with cancer during pregnancy will be subject to emotional stress, which can lead to long-term psychological sequelae. This stress is given by the fear of death, the possible negative effects of cancer treatment on the fetus, the fear that she will not be able to raise their child or by the risk of sterility **[5]**.

The treatment of cervical cancer during pregnancy depends on several variables such as: stage, lympho-vascular space involvement (LVSI), grade, type, the presence of positive lymph nodes, gestational age at diagnosis and not least the wish of the parents **[3-5]**.

CORESPONDENŢĂ: Ioana C. Rotar, e-mail: cristina.rotar@umfcluj.ro
KEY WORDS:cervical cancer, colposcopy, pregnancy, cervical intraepithelial neoplasia

The diagnosis of precursor lesions and cervical cancer during pregnancy

Cervical cytology screening should be performed during the first prenatal visit **[2]**. Emerging data have suggested that the presence of cervical dysplasia and particularly the HPV infection could be associated with the risk of preterm birth and placental abnormalities **[6].** It has also been reported an increased incidence of high-risk strains of HPV (HR-HPV) 16, 18, 31, 35, 45, 51, 52 and 56 in pregnant women when compared to the rest of the female population **[7].**

The risk factors are the same as in nonpregnant women, but with a greater focus placed on young age and multiparity. Squamous metaplasia associated with the first pregnancy can lead to the initiation of postpartum cervical carcinogenesis **[2]**.

Although currently the effect of pregnancy on HPV infection is not fully understood, is now accepted that the immunosuppression characteristic for human pregnancy may cause progression of infection, but also can decrease the ability of the immune system to eliminate the virus from the cells **[1]**. Overall the risk of cervical dysplasia progression during pregnancy is small and usually it remain stationary or can even regress in postpartum **[2]**.

The symptoms are roughly the same as in non-pregnant women. Usually early stages of cervical cancer are often asymptomatic, while more advanced stages could cause symptoms like abnormal vaginal bleeding, vaginal discharge, pelvic pain and dyspareunia **[8]**. Vaginal bleeding is the most frequently encountered symptom for emergency consultation during pregnancy, which can be easily interpreted as an imminent abortion **[8]**. Low back pain or intestinal and urinary symptoms usually occur in more advanced stages and are often misinterpreted as consequences of the uterine growth **[9]**. In advances undiagnosed cases there may be ureteral invasion with hydronephrosis.

The appearance of cervical cancer on clinical exam can be variable: it can be exophytic, growing out of the surface or endophytic with stromal infiltration and minimal surface growth**[8]**.

Cervical cytology. Interpreting a cytological slide can be challenging. Hormonal changes characteristic for normal pregnancy can cause immature metaplasia, basal cell hyperplasia and cellular changes like Arias Stella reaction, which may create difficulties for the differential diagnosis with cervical clear cell carcinoma **[2]**. Moreover the decidual reaction determines the presence of large cells with large nuclei, changes that can be misinterpreted by s inexperienced cytologists as dysplastic cells **[1]**. No differences have been reported regarding the complications (bleeding, miscarriages) between cytobrushes and other types of harvesting brushes **[10]**.

The colposcopy– during pregnancy has to be performed by experienced colposcopists due to its particularity and high difficulty. In cases of abnormal cytology the colposcopy is mandatory and the main goal is to confirm/exclude the diagnosis of in situ or invasive cervical cancer **[2]**. The main problems of colposcopy in pregnancy are:

· the edema, the venous stasis, the friability of the tissue, the pelvic congestion and the vaginal wall protrusion into the examination field may limit the procedure or cause misinterpretation, especially for less experienced examiners **[2]**.

· the increased blood supply can determine a decrease in intensity of the acetowhite epithelium, but the vascular tracts remain well individualized and more easily visible than outside pregnancy **[2]**.

· cervical mucus is thicker, more opaque and adherent, limiting the examination of squamocolumnar junction (SCJ) and transformation zone (TZ). This can be resolved by the application of 5% acetic acid solution that also serves as a mucolytic and the excess of mucus can be removed with a textile sponge**[2]**.

· the development of immature metaplasia can cause some particular images like punctuation or fine mosaic and this can make more difficult the differential diagnosis with LSIL **[2]**.

·SCJ and TZ are easily visible during pregnancy due to the everted mucosa caused by pregnancy hormones **[1, 2]**.

All these cervical changes caused by pregnancy can lead to an overvaluation of dysplastic

lesions diagnosed by colposcopy. An unsatisfactory assessment in the first trimester should be repeated in the second trimester, when the eversion of the mucosa is complete **[1, 2]**.

In conclusion, the role of colposcopy during pregnancy is important in two situations **[1, 2]**:

1) In pregnant women with abnormal cervical cytology with moderate changes, it can diagnose an occult high-grade lesion;

2) In pregnant women with abnormal cervical cytology indicating a severe dysplasia, when it can differentiate the preinvasive lesions from invasive cancer and can guide the biopsy to the most suggestive area.

The biopsy and histopathological examination are necessary sometimes also in pregnancy. Although there is no clear evidence that cervical biopsy during pregnancy has a higher risk of complications, it seems that the risk of bleeding is higher due to local congestion and hyperemia **[10]**. The biopsy is indicated in case of suspicion of high-grade lesion or cancer (ACOG 2013a) and it is recommended to be performed in the second trimester when the risk of bleeding and miscarriage is lower. The number of biopsies should be limited, choosing the most suggestive colposcopic region for severe dysplasia / carcinoma **[2]**. If bleeding occurs, it can be controlled by vaginal packing or local application of silver nitrate or Monsel solution, and if these methods fail we can use suture or electrocoagulation **[1, 2]**.

Cone biopsy for diagnosis should be discussed only when the suspicion of invasion is high and other diagnostic methods have been exhausted. Endocervical curettage is contraindicated in pregnancy **[1, 2]**.

Serum tumor markers are biochemical substances produced by the tumor or by paraneoplastic syndromes. Unfortunately their clinical utility is limited by the lack of specificity and sensitivity, because most tumor markers are associated with several types of tumors **[11]**.

Squamous-cell carcinoma antigen (SCC) – is a nonspecific marker for cervical squamous cell carcinoma, and it's value during pregnancy is similar to that of nonpregnant women **[11]**.

Histopathological grading

According to the WHO there are three categories of epithelial tumors of the cervix: squamous (which accounts for approximately 70%–80% of cervical cancers), adenocarcinoma (10%–15% of cervical cancers), and other epithelial tumors including neuroendocrine tumors and undifferentiated carcinoma **[8]**. Other rare histological types Mesenchymal tumours (Leiomyosarcoma, Sarcoma botryoides, Angiosarcoma), mixed epithelial and mesenchymal tumours (Carcinosarcoma, Wilms tumor) or Melanocytic tumours (Blue naevus, malignant melanoma) like appear exceptional during pregnancy.

The imaging staging of cervical cancer in pregnancy

Clinical staging in pregnancy is difficult and tends to underestimate the extent of the disease because the parametrial involvement is hard to be established due to water retention and uterine growth. The imaging staging gives a better accuracy compared to clinical staging.

Ultrasound and Doppler ultrasound can be used without restriction throughout pregnancy. Ultrasound is the examination of choice for the imaging of pelvic and abdominal pathology, but its role in cervical cancer staging is limited **[5, 12]**.

MRI can also be used throughout pregnancy, but contrast agents should be avoided. Pelvic MRI imaging offers a good staging, but lymphadenectomy remains gold standard in diagnosing the extent of the disease **[12]**.

Sentinel node with Technetium 99 may be used with caution if the other diagnostic methods have been exhausted **[5]**. Sentinel node with Technetium 99 is allowed during pregnancy but it's utility for cervical cancer it's still under investigation, the main indication for its use remains vulvar cancer **[9, 12]**.

CT, PET-CT must be avoided if the woman wants to carry on the pregnancy **[5, 12]**

Cervical cancer staging – is according with FIGO 2010 clasiffication and is the same as for nonpregnant women **[13].**

The management of invasive cervical cancer in pregnancy

The management of cervical cancer during pregnancy depends on many factors such as stage of disease, gestational age, the couple's desire and the therapeutic possibilities. Early stages, diagnosis in the 2nd or 3rd trimesters can give the couple a chance to keep the pregnancy, while the diagnosis in advanced stages or in early pregnancy results in making important and sometimes difficult decisions. A particular situation occurs when an early diagnosis of cervical cancer in established in the first trimester, and the couple will have to decide between maintaining the pregnancy and the woman's obstetrical future.

Surgery during the first trimester does not appear to increase the risk of birth defects, but the risk of miscarriage increases. Therefore, when it's possible, surgery should be deferred until the second trimester, when the risks are lowest.

Large conization is indicated for early stages of cervical cancer like stage IA1 without lymphovascular space invasion or CIS. The most favourable time for cervical conisation is in the second trimester, between 14 and 20 weeks **[14]**, because during pregnancy the risk of bleeding increases. The procedure can be performed by loop electrosurgical excisional procedure (LEEP) or by cold knife conization.

Radical trachelectomy –also known as cervicectomy, is a surgical removal of the uterine cervix and the vaginal cuff **[15]**. Normally this procedure takes place along with the lymphadenectomy or single node biopsy (SNB) to assess the lymph nodes involvement. There are two methods of making this surgical procedure: radical vaginal trachelectomy (RVT), also known as the Dargent operation and radical abdominal trachelectomy (RAT) **[16]**. This procedure is indicated for lesions smaller than 2 cm **[17]**, but there are studies that are trying to evaluate the opportunity of radical trachelectomy for tumours 2-4 cm, but so far the results have been conflicting **[18, 19]**.

For confirmed stage I cervical cancer in women seeking maintaining the pregnancy or the reproductive function, the surgery of choice is conization or radical trachelectomy with or without bilateral pelvic laparoscopic lymphadenectomy (for a diagnostic and not therapeutic purpose).

The most common intraoperative complication of radical trachelectomy (RT) are urinary tract lesions, vascular lesions, lymphocele and bleeding in the parameters with suprapubic hematoma **[20]**. Late postoperative complications that can be found with a higher frequency are: dysmenorrhea (24%) excessive vaginal bleeding (14%), chronic pelvic pain, dyspareunia, vulvar oedema, hypotonic bladder, amenorrhea, cervical stenosis and urinary tract infections **[20]**.

Radical trachelectomy has a higher risk of bleeding and the risk of miscarriage is up to 32%, so nowadays wide conization has become the preferred method of treatment during pregnancy **[21]**.

It seems that the results of a wide conizations are similar to those of a radical trachelectomy, especially if it succeeds in achieving safety margins of approximately 1 cm **[22]**.

Also there is no consensus regarding the time that the woman must wait after radical trachelectomy to conceive a baby, this interval ranging from 6 months to 1 year, or even 2 years after some authors **[21]**.

For stage IA1 confirmed on cone biopsy it is possible and safe to continue the pregnancy and deliver vaginally and the definitive therapy will be effectuated after 6 weeks postpartum. **[28]**

For stages IA2 and IIA, diagnosed in the first half of pregnancy the indication is immediate treatment, but the decision depends also of the couple desire to continue the pregnancy or not. If the diagnostic is made in the second half there is a consensus that the pregnancy can be continued until the pulmonary maturity of the fetus, unless if there is a bulky lesion on the cervix. In more advanced stages immediate treatment is mandatory.

Lymph node biopsy is important in pregnant women with cervical cancer at stage IA2–IB1, where it should be performed first. If pelvic lymphadenectomy cannot be performed or if the patient doesn't agree with the surgery, neoadjuvant

chemotherapy will be indicated but the results and the prognosis will be worse, the risk of loco-regional recurrence or distant metastasis being increased **[9]**. If after pelvic lymphadenectomy the lymph nodes are negative, the rest of the treatment will be postponed after birth, but if the disease is extended to nodes, neoadjuvant chemotherapy or pregnancy termination is required **[9]**.

Radical vaginal trachelectomy RVT is indicated in stage FIGO IA1 with LVSI +, IA2 and IB1, in tumour less than 2 cm, with no lymph node metastases and tumour localised only at the cervix, confirmed by IRM.

The possibilities of treatment for women with cervical cancer stage I-II diagnosed in the second trimester of pregnancy that wish to continue the pregnancy are presented in Figure 2.

For stages IIB and more, abortion and standard oncological treatment is indicated in cases when the woman does not want to maintain the pregnancy **[13]**.

Standard treatment (radical hysterectomy or radiochemotherapy) is used when lymph nodes are positive. Standard treatment is considered if there is poor response to induction chemotherapy. At more advanced stages (IIA2–IIIB), classical therapy (radical hysterectomy or radiochemotherapy) should be used when appropriate gestational age is reached **[13]**. Radical hysterectomy with pelvic lymphadenectomy is the treatment recommended for invasive carcinoma in most patients with stage I and early stage IIA lesions **[23]**. Before 20 weeks, hysterectomy is usually performed with the fetus in situ. In later pregnancy, caesarean section is normally performed first.

Neoadjuvant Chemotherapy. Both in pregnancy and in young women that wish the reproductive function preservation neoadjuvant chemotherapy is indicated for tumours > 2 cm, invasion of LVSI, positive lymph nodes after pelvic lymphadenectomy **[9, 20]**.

During pregnancy we can use Cisplatin (75mg / m^2) +/- Paclitaxel (175 mg / m^2) in cycles every 3 weeks, because their association has a better effect compared with Cisplatin alone **[24]**. Carboplatin can be an option, but with higher risk of maternal-fetal toxicity and a weaker response to neoadjuvant treatment **[24]**, but Topotecan and Gemcitabine should be avoided due to insufficient studies **[9]**.

Radiotherapy and Brachytherapy are generally contraindicated during pregnancy because of the risk of miscarriage or fetal death in utero **[5, 21]**. In advances cases diagnosed in the first trimester, when patients do not wish the continuation of pregnancy, external radiotherapy can be used and usually abortion occurs. If the abortion does not occurs, D&C is performed.

Delivery. The effects of a vaginal delivery through a cancerous cervix are unknown. For this reason, the mode of delivery is controversial, especially for small, early-stage lesions. In cases with bulky or friable lesions an important haemorrhage can occur during vaginal delivery. For these reasons most authors prefer the caesarean delivery. There are also opinions that favour the use a classical hysterotomy incision to avoid the risk of cutting through the tumour **[28].**

Prognosis.

The survival rates of pregnant and non-pregnant women with invasive cervical cancer in early stages are similar **[25]**.

Oncological prognosis. RVT is an effective method of preserving fertility in young patients in early stage of cervical cancer, maintaining a balance between oncological safety and future obstetrical outcome **[26]**. The 5-year survival after RVT is 95-97%, similar to that after radical hysterectomy for the same type of lesions **[20]**, but the risk of recurrence is higher in tumours with diameter over 2 cm, LVSI invasion, stromal invasion> 1 cm positive lymph nodes **[20]**.

Obstetrical prognosis. Regarding the possible obstetric complications, Kim et al reported 10 cases of cervical stenosis and 2 cases of erosion associated cerclage in the 35 cases studied **[27]**.

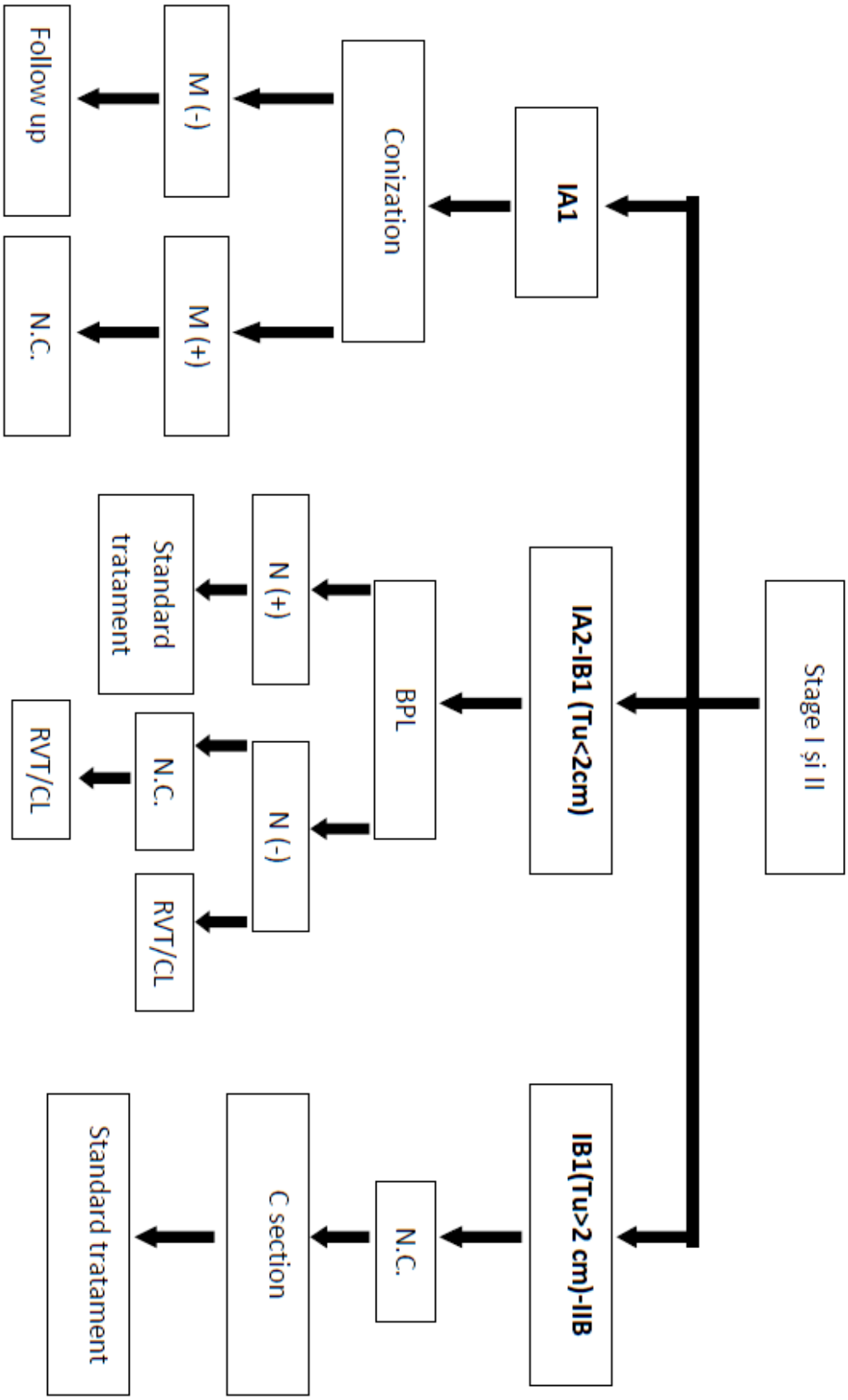

Figure 1. Treatment of incipient cervical cancer in 2nd trimester in patients that wish maintaining the pregnancy. (-) negative; (+) positive; BPL= bilateral pelvic lymphadenectomy; RVT = Radical vaginal trachelectomy; CL =Wide conization; M=Margins; N = Lymph nodes, N.C. = Neoadjuvant Chemotherapy (NCCN Guidelines 2015).

However the most common complications after RVT remain preterm birth and premature rupture of membranes, the mechanism being caused either by cervical incompetence either by the higher risk of local infection which occurs due to insufficient production of mucus **[28]**.

Regarding the route of delivery after RVT, it seems that caesarean section is widely accepted, the only remaining disagreement being about the type of incision. Although some authors claim that corporeal vertical incision is the wright choice, it seems that it has severe complications and high risk of bleeding, and a high transverse incision avoids these problems and is equally effective **[26]**.

Conclusions

The diagnosis of cervical cancer during pregnancy is a delicate issue that puts pressure on both the family and the medical team. Treatment must be conducted by a multidisciplinary team which should include an obstetrician, a neonatologist, an oncologist, a cancer surgeon, a radiotherapist as well as an expert in maternal-fetal medicine.

The decision to continue or to interrupt the pregnancy and start the oncological treatment should be taken together by the family and medical team after explaining all maternal-fetal risks and the opportunities of patient's treatment. Certainly this decision is influenced by gestational age, stage of disease, the patient's obstetrical history and the desire to preserve reproductive function, but the final decision lies with the couple.

References

1. Origoni M, Salvatore S, Perino A, Cucinella G, Candiani M. Cervical Intraepithelial Neoplasia (CIN) in pregnancy: the state of the art. Eur Rev Med Pharmacol Sci. 2014;18(6):851-60.
2. Apgar BS, Brotzman GL, Spitzer M. Colposcopy, principles and practice : an integrated textbook and atlas. Philadelphia: Saunders/Elsevier,; 2008.
3. Marnitz S, Kohler C, Oppelt P, Schmittel A, Favero G, Hasenbein K, et al. Cisplatin application in pregnancy: first in vivo analysis of 7 patients. Oncology. 2010;79(1-2):72-7.
4. Lanowska M, Kohler C, Oppelt P, Schmittel A, Gottschalk E, Hasenbein K, et al. Addressing concerns about cisplatin application during pregnancy. J Perinat Med. 2011;39(3):279-85.
5. Amant F, Van Calsteren K, Halaska MJ, Beijnen J, Lagae L, Hanssens M, et al. Gynecologic cancers in pregnancy: guidelines of an international consensus meeting. Int J Gynecol Cancer. 2009;19 Suppl 1:S1-12.
6. Zuo Z, Goel S, Carter JE. Association of cervical cytology and HPV DNA status during pregnancy with placental abnormalities and preterm birth. Am J Clin Pathol. 2011;136(2):260-5.
7. Fife KH, Katz BP, Roush J, Handy VD, Brown DR, Hansell R. Cancer-associated human papillomavirus types are selectively increased in the cervix of women in the first trimester of pregnancy. Am J Obstet Gynecol. 1996;174(5):1487-93.
8. Colombo N, Carinelli S, Colombo A, Marini C, Rollo D, Sessa C, et al. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2012;23 Suppl 7:vii27-32.
9. Han SN, Verheecke M, Vandenbroucke T, Gziri MM, Van Calsteren K, Amant F. Management of gynecological cancers during pregnancy. Curr Oncol Rep. 2014;16(12):415.
10. Stillson T, Knight AL, Elswick RK, Jr. The effectiveness and safety of two cervical cytologic techniques during pregnancy. J Fam Pract. 1997;45(2):159-63.
11. Han SN, Lotgerink A, Gziri MM, Van Calsteren K, Hanssens M, Amant F. Physiologic variations of serum tumor markers in gynecological malignancies during pregnancy: a systematic review. BMC Med. 2012;10:86.
12. Peccatori FA, Azim HA, Jr., Orecchia R, Hoekstra HJ, Pavlidis N, Kesic V, et al. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 Suppl 6:vi160-70.
13. Koh WJ, Greer BE, Abu-Rustum NR, Apte SM, Campos SM, Cho KR, et al. Cervical Cancer, Version 1.2016. J Natl Compr Canc Netwo. 2016;14(1).
14. Van Calsteren K, Vergote I, Amant F. Cervical neoplasia during pregnancy: diagnosis, management and prognosis. Best Pract Res Clin Obstet Gynaecol. 2005;19(4):611-30.
15. Tanguay C, Plante M, Renaud MC, Roy M, Tetu B. Vaginal radical trachelectomy in the treatment of cervical cancer: the role of frozen section. Int J Gynecol Pathol. 2004;23(2):170-5.
16. Abu-Rustum NR, Sonoda Y. Fertility-sparing radical abdominal trachelectomy for cervical carcinoma. Gynecol Oncol. 2007;104(2 Suppl 1):56-9.
17. Abu-Rustum NR, Sonoda Y, Black D, Levine DA, Chi DS, Barakat RR. Fertility-sparing radical abdominal trachelectomy for cervical carcinoma: technique and review of the literature. Gynecol Oncol. 2006;103(3):807-13.
18. Lanowska M, Mangler M, Speiser D, Bockholdt C, Schneider A, Kohler C, et al. Radical vaginal trachelectomy after laparoscopic staging and neoadjuvant chemotherapy in women with early-stage cervical cancer over 2 cm: oncologic, fertility, and neonatal outcome in a series of 20 patients. Int J Gynecol Cancer. 2014;24(3):586-93.
19. Lintner B, Saso S, Tarnai L, Novak Z, Palfalvi L, Del Priore G, et al. Use of abdominal radical trachelectomy to treat cervical cancer greater than 2 cm in diameter. Int J Gynecol Cancer. 2013;23(6):1065-70.

20. Schneider A, Erdemoglu E, Chiantera V, Reed N, Morice P, Rodolakis A, et al. Clinical recommendation radical trachelectomy for fertility preservation in patients with early-stage cervical cancer. Int J Gynecol Cancer. 2012;22(4):659-66.
21. Amant F, Halaska MJ, Fumagalli M, Dahl Steffensen K, Lok C, Van Calsteren K, et al. Gynecologic cancers in pregnancy: guidelines of a second international consensus meeting. Int J Gynecol Cancer. 2014;24(3):394-403.
22. Rob L, Skapa P, Robova H. Fertility-sparing surgery in patients with cervical cancer. Lancet Oncol. 2011;12(2):192-200.
23. American College of Obstetricians Gynecologists. ACOG Committee Opinion No. 463: Cervical cancer in adolescents: screening, evaluation, and management. Obstet Gynecol. 2010;116(2 Pt 1):469-72.
24. Zagouri F, Sergentanis TN, Chrysikos D, Bartsch R. Platinum derivatives during pregnancy in cervical cancer: a systematic review and meta-analysis. Obstet Gynecol. 2013;121(2 Pt 1):337-43.
25. Pavlidis NA. Coexistence of pregnancy and malignancy. Oncologist. 2002;7(4):279-87.
26. Ma LK, Cao DY, Yang JX, Liu JT, Shen K, Lang JH. Pregnancy outcome and obstetric management after vaginal radical trachelectomy. Eur Rev Med Pharmacol Sci. 2014;18(20):3019-24.
27. Kim CH, Abu-Rustum NR, Chi DS, Gardner GJ, Leitao MM, Jr., Carter J, et al. Reproductive outcomes of patients undergoing radical trachelectomy for early-stage cervical cancer. Gynecol Oncol. 2012;125(3):585-8.
28. Jolley JA, Battista L, Wing DA. Management of pregnancy after radical trachelectomy: case reports and systematic review of the literature. Am J Perinatol. 2007;24(9):531-9.