Fertility and pregnancy after cervical procedures

The challenge of achieving good outcomes

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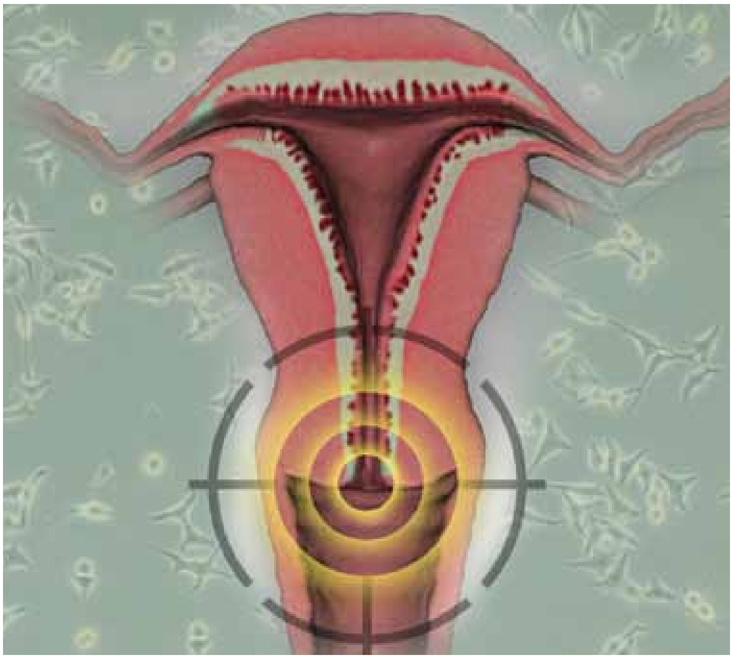

Since the development and wide implementation of cervical cancer screening programs, cervical cancer rates have decreased by up to 80%.[1] Screening has increased the identification of cervical intraepithelial neoplasia (CIN), carcinoma in situ (CIS), and cervical dysplasia in young women during their reproductive years. In fact, the International Federation of Gynecologists and Obstetricians (FIGO) 2006 annual report showed that 49% of all cases of cervical carcinoma worldwide occurred in women younger than 49 years.[2] This is a challenging situation given that the age of nulliparous women has increased.[2] The data point to the need for conservative fertility-preserving management of cervical dysplasia and carcinoma, especially in preinvasive and microinvasive disease.

While the therapies used to treat cervical disease have high success rates, they also carry a risk for long-term morphologic damage that may in turn result in gynecologic and obstetric complications, including cervical stenosis, preterm delivery, and low birth weight. This article reviews the ablative and excisional procedures used to treat cervical disease, their potential adverse impact on reproductive and fertility outcomes, and what guidance the literature offers regarding tailoring treatment to minimize residual disease and improve the chances of good gynecologic and obstetric outcomes.

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Treatments for cervical disease

Treatment of CIN can include eradication of the transformation zone (TZ) by ablation or excision, depending on the nature and extent of disease. Ablative methods include cryotherapy, laser vaporization, and electrocoagulation diathermy. Excisional methods include laser conization, cold knife conization, and large loop excision of the transformation zone (LLETZ) or loop electrosurgical excision procedure (LEEP). (See the **TABLE** for a description of these procedures.)

Excisional techniques preserve the ability to obtain an optimal histologic evaluation, including examination of the margins of the lesion, while also preserving fertility. Additional advantages include the low cost, the outpatient procedure and fast treatment time, the simplicity of the procedure, and a good compliance rate of patients in the outpatient setting. For patients with high-grade lesions, excision is the standard treatment.[3] Excision techniques are well accepted because of their success in treating disease. For example, the treatment success of cold knife conization is reported as high as 90% to 94%.[4,5] Treatment success of LLETZ is reported between 91% and 98%.[6-11]

In patients with early-stage cervical cancer (stage FIGO IA-IB1), radical vaginal

TABLE Fertility-preserving treatments for cervical dysplasia or cancer

	Technique	Description
ABLATIVE METHODS	Electrocoagulation diathermy	Electrocoagulation diathermy or electrocautery uses electricity to destroy the cervical lesion. The lesion is coagulated with a ball electrode at a power setting of 40-80 watts to a depth of 7 mm around the cervical canal.
	Cryotherapy	Cryotherapy involves freezing the cancerous lesion with a metal probe that is cooled with refrigerants. The probe is applied to the tissue and kept in contact with the tissue until an ice "ball" forms. After the tissue has visibly thawed, it is usually frozen a second time to ensure a thorough treatment.
	Laser vaporization	A laser beam is used to destroy the abnormal tissue. Laser destruction of tissue can be controlled by the length of exposure. Defocusing the beam permits photocoagulation of bleeding vessels in the cervical wound.
EXCISIONAL METHODS	Large loop excision of the transformation zone (LLETZ) or loop electrosurgical excision procedure (LEEP)	The cervix is infiltrated with a local anesthetic and vasoconstrictive agent. The loop is placed with slight pressure at the edge of the lesion and the cutting mode is activated. When the loop has advanced 5-6 mm into the tissue, it is drawn through the tissue with almost no force. A depth of 7-8 mm is reached toward the cervical canal. The pass through the tissue can be made from above to below or from one side to the other. For hemostasis, the cut surface is coagulated with the ball electrode.
	Cold knife conization (CKC)	The cervix is stained with Lugol's solution to define the base of the cone and is infiltrated with 10-20 mL of dilute solution of vasopressin. Beginning at the posterior lip, a 5-cm–deep sagittal incision is made with a small, straight scalpel. Then a slender pointed angled knife is used to direct the plane of the incision toward the cervical canal and define a cone. A Hegar probe is placed in the cervical canal to ensure that the tip of the cone encompasses the cervical canal. Any remaining tissue bridges are snipped with scissors. The cut surface of the cervix is coagulated with a conical thermocoagulator for 15-30 seconds or closed with a Sturmdorf suture.
	Laser conization	The exocervical margins are outlined with 0.5-1 mm dots produced by laser energy at a power setting of 20-50 watts. A laser incision is performed to connect the dots and extended to a depth of 3-5 mm. The procedure is completed using laser, scalpel, and Mayo scissors.
	Radical vaginal trachelectomy (RVT)	The surgical technique includes making a "vaginal cuff," opening the ventrolateral dry spaces (vesicovaginal space and paravesical spaces), and then dividing the bladder pillars (vesicouterine ligaments) to identify the ureters and uterine arteries. After opening the Douglas pouch, the rectum pillars (rectouterine ligaments) are divided. At this time, the paracervical ligaments, the ventral and dorsal aspects of which are visible, can be divided between 2 clamps, the most lateral being placed 2 cm outside the vaginal cuff. The last step of the procedure involves dividing the uterus, which is transected 5 mm underneath the isthmus. The reconstruction includes closing the Douglas pouch, putting a cerclage around the isthmus, and reanastomosing the vagina to the isthmus. No drain is left in place. A Foley catheter is inserted for 2-6 days

trachelectomy (RVT) with laparoscopic pelvic lymphadenectomy may be a valid surgical alternative to radical hysterectomy; this procedure preserves reproductive potential by removing only the cervix plus some parametrial tissue and a margin of vagina.[12] The oncologic outcome is thought to be comparable to traditional surgery for early-stage disease.[13]

Ablation treatments

Cryotherapy, laser vaporization, and diathermy have in common the principle that the entire TZ is destroyed to a depth of about 7 mm.[14] Destruction of epithelium precludes histologic evaluation; therefore, this treatment is advisable when colposcopy is satisfactory and when there is no suspicion of glandular or invasive disease. Treatment success, in terms of disease recurrence, after laser vaporization is approximately 95%.[15] Success of treatment with cryotherapy is between 77% and 93%.[16-18] The literature suggests that long-term morbidity is less concerning after ablative cervical procedures than after excisional procedures.

In general, there does not appear to be an association between ablative procedures and infertility. In 1995, Spitzer et al reported that cervical laser surgery was not associated with impairments in fertility or with preterm labor.[19] A 2006 meta-analysis found that laser ablation was not significantly associated with adverse effects on pregnancy outcomes or on fertility (RR=0.87; 95% CI, 0.63-1.20).[20] More recently, another meta-analysis demonstrated that, although the risk associated with ablative treatment was not increased, there was a trend toward increased perinatal mortality in patients who had been treated with diathermy (RR=1.54).[21] In addition, while laser ablation and cryotherapy were not associated with preterm delivery, a significantly higher rate of low birth weight was observed in women treated with diathermy.[21]

Excisional treatments

LEEP or LLETZ

The LLETZ procedure utilizes a high current in a very thin wire loop that cuts the tissue, producing minimal thermal damage to the surrounding tissue.[22] The depth of the cervical excision is between 0.7 and 1.5 cm. Typically used to treat CIN2 or CIN3, this procedure is reserved for patients who are thought to be at higher risk for carcinogenesis yet may be managed more conservatively, as the disease is still preinvasive.

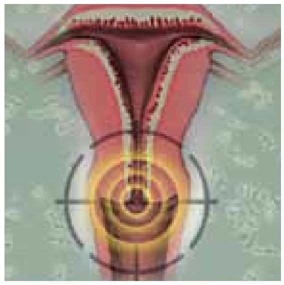
Data are conflicting regarding the impact of LLETZ or LEEP on pregnancy risks. A meta-analysis published in 2006 showed that LLETZ was significantly associated with preterm delivery (RR=1.70; 95% CI, 1.24-2.35), low birth weight (RR=1.82), and preterm premature rupture of membranes (PPROM) (RR=2.69).[20] However, many earlier studies found that cervical excision treatment, including LLETZ, was not associated with preterm delivery or PPROM.[23-25] These conflicting results may be explained by poor study design, small sample sizes, and several confounding factors, such as depth of the cervical excision or the presence of other risk factors for pregnancy outcome (smoking, multiple sex partners, or sexually transmitted disease).[26] A recent study in Brazil attributed most of these clinical consequences to cervical stenosis.[27] However, this study did not prove that cervical stenosis is necessarily a prognostic factor for obstetric outcome: the 7.66% incidence in the study population was not higher than the percentage described in the literature for excision electrosurgical treatments. It is possible, however, that hemorrhagic complications requiring cauterization or suture may cause infertility, preterm labor, or PPROM.[27]

A meta-analysis by Kyrgiou et al concluded that fertility is not impaired after LLETZ.[20] Other studies demonstrate that LLETZ does not have a role in first- or second-trimester miscarriage, probably because the procedure removes a smaller amount of cervical tissue.[24,25] In general, a literature review reveals a lack of good evidence regarding the effect of cervical excision treatments on fertility.

Cold knife conization

When endocervical assessment shows CIN and colposcopy is not satisfactory, and/or if cytology or colposcopy examination suggests cancer, ablative therapy is not appropriate.[28] To preserve fertility in young women, the cold knife conization (CKC) technique was developed in 1985.[29]

This conservative approach is highly effective in controlling preinvasive disease. While CKC provides the cleanest specimen margins for further histologic study, it is typically asso-



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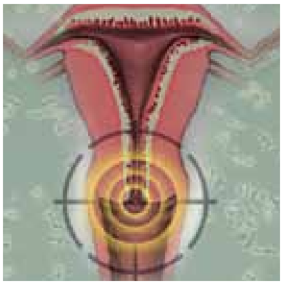

ciated with more bleeding than laser or LEEP; in some cases, general anesthesia is required. A recent Cochrane Review reported treatment success (in terms of no residual disease) of 90% to 94% in nonrandomized studies.[30]

Several reproductive concerns are associated with CKC, including a significant association with second-trimester miscarriage. A study comparing pregnancies in 414 patients before and after CKC reported a rate of late spontaneous miscarriages in treated patients 7 times greater than before surgery.[31] This complication increases based on the size of cone biopsy.[31] Conversely, a prospective study by Mathevet et al found no increase of early or late miscarriage or PPROM.[24]

A recent meta-analysis revealed that only CKC was consistently associated with serious adverse pregnancy outcomes.[21] Unavoidably, the CKC procedure removes more cervical tissue than other techiniques.[20] Finally, a recent meta-analysis that included data from 27 studies found a significant association between CKC and preterm delivery (gestation <32/34 weeks) (RR=2.59), low birth weight (RR=2.53), and perinatal mortality (RR=2.87).[21]

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Laser conization

Laser conization employs a highly focused laser spot to make a cervical external side circular incision to a depth of 1 cm. Hemostasis is generally guaranteed through laser coagulation by defocusing the beam. The advantages of this technique are more accurate tailoring of cone size, less cervical trauma, and low blood loss. A disadvantage is that the cone biopsy specimen receives thermal damage, precluding histologic evaluation of margins. A Cochrane Review reported laser conization treatment success as 93% to 96% in nonrandomized studies.[30] The relative risk of perinatal mortality associated with laser conization was heterogeneous.[21] The frequency of cervical stenosis in patients who underwent laser conization has been reported as 4% to 11%.[32,33]

Radical vaginal trachelectomy

In select young women with stage I cervical cancer who desire future fertility, RVT has become an acceptable alternative to radical hysterectomy.[34,35]

While surgical morbidity appears to be lower in patients who undergo conservative approaches because the procedures are less protracted,[36] patients who have an RVT often present with dysmenorrhea (24%), irregular bleeding (17%), excessive vaginal discharge (14%), and isthmic stenosis (10%) with or without amenorrhea.[37] A recent comparative study confirmed that disease recurrence rate and death rate in patients treated with RVT were comparable to those of patients with equivalent-sized lesions who underwent radical abdominal hysterectomy.[38]

Cervical incompetence caused by RVT presents important obstetric consequences. Second-trimester miscarriage in RVT patients is twice the rate found in the general population (8.6% vs 4%), while the rate of first-trimester miscarriage is comparable to that in the general population (16% to 20%). Preterm labor is more frequent, with the premature birth rate varying among different studies, likely due to the variability in the amount of cervix excised. In 2005, Plante et al showed that 8 of 50 pregnancies (16%) ended prematurely (<37 weeks).[34] In another study of RVT for early-stage cervical cancer, preterm delivery occurred in 7 of 9 live births.[39]

The estimated cumulative fertility rate in patients who underwent RVT has been reported as 55%.[40] This is probably due to cervical stenosis, absence of cervical mucus, subclinical infections, and adhesion formation. Cervical stenosis occurs in about 15% of RVT patients. Although this complication is often asymptomatic, patients sometimes present with pelvic pain and hematometra. Assisted reproduction techniques (ART) may be helpful for these women. Jolley et al reported 200 pregnancies post-RVT and a second-trimester spontaneous abortion rate of 9.5% (19/200).[41] Of the 200 pregnancies, there were 49 (25%) preterm deliveries (24 to 37 weeks' gestation) and 84 term births (>37 weeks).[41] Compared with the US incidence of preterm birth (13%),[42] patients who underwent RVT have a 2 times greater chance of preterm delivery. The risk for PPROM in these patients appears to be higher than in the general population.[39, 43,44]

Possible mechanisms that compromise cervical function

Two recent meta-analyses demonstrated that cervical excisional procedures are associated with adverse pregnancy outcomes.

These outcomes may be caused by the cervical modifications after surgery; in other words, the loss of cervical tissue may compromise mechanical function. The new collagen formed in scar tissue may be more fragile and react abnormally to hormonal changes of pregnancy. Furthermore, conization removes endocervical glands, causing a decrease in mucus, which may potentially compromise both fertility and pregnancy outcome. For instance, this might lead to endocervical infections, which contribute to PPROM and preterm labor.[45]

Amount of tissue excised. A greater volume of cervical tissue excised could relate to the occurrence of partial or complete obstruction of the cervical canal; cervical stenosis often is associated with dysmenorrhea, amenorrhea, and infertility. In the literature, there is a lack of consensus regarding the definition of cervical stenosis, which may account for the high variability in incidence (0% to 25.9%) observed. A study in Brazil found that hemorrhagic complications during the immediate pre- or postoperative period, which led to suturing of operative wounds or intense cauterization, were found to be associated with subsequent cervical stenosis.[27]

Depth of surgical incision. Depth of conization and the volume of cervical tissue removed have been evaluated as a risk factor for adverse pregnancy outcome and infertility. The proportion of the total cervical volume or endocervical canal removed seems to be more important than the actual depth of excision. A meta-analysis showed a relative risk of 2.61 for preterm delivery with a core depth of cone specimen greater than 10 mm (95% CI).[21] The retrospective studies included in this meta-analysis presented wide variations in the loop sizes used and, consequently, the cone volume removed. This may explain the wide range of relative risks (from 0.46 to 7.00) and the nonsignificant pooled effect of loop excision on perinatal mortality.

A paper presented at the British Society for Colposcopy and Cervical Pathology meeting in 2009 described 353 women who underwent LLETZ in the same hospital; nearly 10% had a preterm delivery.[46] The authors examined the correlation between volume, length, and thickness of removed zone with the risk of preterm delivery. There was a more than 3-fold increase in the risk of preterm delivery if the excision volume exceeded 6 cm^3 (RR=3.17) when compared to small excisions defined as volumes of less than 3 cm. There has not been an association between length of excision, but between large-volume excision and preterm delivery.[46] Therefore, the concept that the large amount of volume excised increases the risk for preterm delivery is plausible.

Timing of pregnancy after surgery. Time to pregnancy after excision may also be important. Himes and Simhan demonstrated that in women who underwent conization, those with a subsequent preterm birth had a shorter conization-to-pregnancy interval (337 days) than women with a subsequent term birth (581 days) (P=.004).[47] These data are significant, and women of reproductive age who must have a conization procedure can be counseled that conceiving within 2 to 3 months of the procedure may be associated with an increased risk of preterm birth. Timing could be an important factor for therapeutic or prophylactic management.[47]

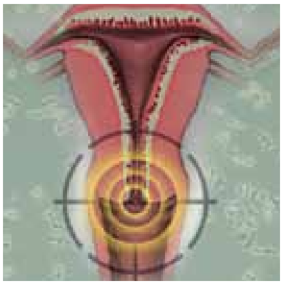
Cervical length. Identifying predictive factors of adverse pregnancy outcome in patients treated with cervical surgery would be valuable. Berghella et al showed that a cervical length measured by ultrasound could be predictive of preterm birth if its value was less than 25 mm in patients who underwent cervical procedures.[48] Another study confirmed that cervical length is predictive of preterm delivery.[49] This study found that at 24 to 30 weeks' gestation, women with prior cervical surgery had cervical lengths similar to women with a previous spontaneous preterm birth.

Preventing preterm birth

One might consider screening women who have had prior cervical surgery. Between 16 and 18 weeks' gestation might be an optimal period to start prophylactic therapy with progesterone. Meis et al showed that progesterone (17-alpha-hydroxyprogesterone caproate, or 17P) could decrease the recurrence of preterm birth when administered starting between 16 and 20 weeks and continuing until delivery or 36 weeks' gestation.[50] Berghella et al reported that 17P had no additional benefit for preventing preterm birth in women who had prior spontaneous preterm birth and received ultrasound-indicated cerclage for cervical length <25 mm.[51] Instead, in women

KEY POINT

Women of reproductive age who must have a conization procedure can be counseled that conceiving within 2 to 3 months of the procedure may be associated with an increased risk of preterm birth.



who did not have cerclage, 17P reduced previable birth and perinatal mortality.

Few studies have examined the impact of cerclage after cervical procedures. Zeisler in 1997 concluded that prophylactic cerclage does not prevent premature delivery and may induce preterm uterine contractions.[52] While there are presently no specific guidelines regarding cerclage placement, cerclage is still an option for select patients.

Counseling patients based on current evidence

For women of reproductive age who require cervical procedures, gynecologists must explain the risks and benefits of ablative and excisional methods. Patients should be informed about the potential impact of cervical procedures on future fertility and/or pregnancy. Surgical treatment should be tailored to minimize residual disease and decrease the chances of poor gynecologic and obstetric outcome.

KEY POINT

Surgical treatment should be tailored to minimize residual disease and decrease the chances of poor gynecologic and obstetric outcome.

In young women with CIN and a very low risk of progression, the option of "wait and see" with close follow-up should be considered. According to the literature, the risks in pregnant women with a history of prior excision should be considered. The lack of controlled prospective studies makes it difficult to define the risk factors, however, and, therefore, implement preventive management of adverse pregnancy outcomes or infertility. Unfortunately, the literature shows interesting data but conflicting results. Large prospective studies are needed so that guidelines can be developed for prevention and management of adverse gynecologic and obstetric outcomes after cervical procedures. ■

REFERENCES

1. Clifford GM, Gallus S, Herrero R, et al. Worldwide distribution of human papillomavirus types in cytologically normal women in the International Agency for Research on Cancer HPV prevalence surveys: a pooled analysis. Lancet. 2005;366:991-998.
2. Quinn MA, Benedet JL, Odicino F, et al. Carcinoma of the cervix uteri. FIGO 6th Annual Report on the Results of Treatment in Gynecological Cancer. Int J Gynaecol Obstet. 2006;95(suppl 1):S43-S103.
3. Alvarez RD, Helm CW, Edwards RP, et al. Prospective randomized trial of LLETZ versus laser ablation in patients with cervical intraepithelial neoplasia. Gynecol Oncol. 1994;52:175-179.
4. Bostofte E, Berget A, Falck Larsen J, et al. Conization by carbon dioxide laser or cold knife in the treatment of cervical intra-epithelial neoplasia. Acta Obstet Gynecol Scand. 1986;65:199-202.
5. Tabor A, Berget A. Cold-knife and laser conization for cervical intraepithelial neoplasia. Obstet Gynecol. 1990;76:633-635.
6. Prendiville W, Cullimore J, Norman S. Large loop excision of the transformation zone (LLETZ): a new method of management for women with cervical intraepithelial neoplasia. Br J Obstet Gynaecol. 1989;96:1054-1060.
7. Bigrigg A, Haffenden DK, Sheehan AL, et al. Efficacy and safety of large-loop excision of the transformation zone. Lancet. 1994;343:32-34.
8. Luesley DM, Cullimore J, Redman CW. Loop diathermy excision of the cervical transformation zone in patients with abnormal cervical smears. BMJ. 1990;300:1690-1693.
9. Whiteley PF, Oláh KS. Treatment of cervical intraepithelial neoplasia: experience with the low-voltage diathermy loop. Am J Obstet Gynecol. 1990;162:1272-1277.
10. Murdoch JB, Morgan PR, Lopes A, Monaghan JM. Histological incomplete excision of CIN after large loop excision of the transformation zone (LLETZ) merits careful follow up, not retreatment. Br J Obstet Gynaecol. 1992;99:990-993.
11. Shepherd JH. Challenging dogma: radical conservation surgery for early stage cervical cancer in order to retain fertility. Ann R Coll Surg Engl. 2009;91:181-187.
12. Dargent D, Martin X, Sacchetoni A, Mathevet P. Laparoscopic vaginal radical trachelectomy: a treatment to preserve the fertility of cervical carcinoma patients. Cancer. 2000;88:1877-1882.
13. Dursun P, Ayhan A, Kuscu E. New surgical approaches for the management of cervical carcinoma, Eur J Surg Oncol. 2008;34:487-496.
14. Benedet JL, Nickerson KG, Anderson GH. Cryotherapy in the treatment of cervical intraepithelial neoplasia. Obstet Gynecol. 1981;58:725-729.
15. Jordan JA, Woodman CB, Mylotte MJ, et al. The treatment of cervical intraepithelial neoplasia by laser vaporization. Br J Obstet Gynaecol. 1985;92:394-398.
16. Kaufman RH, Irwin JF. The cryosurgical therapy of cervical intraepithelial neoplasia. III. Continuing follow-up. Am J Obstet Gynecol. 1978;131:381-388.
17. Hatch KD. Cryotherapy. Baillieres Clin Obstet Gynaecol. 1995;9:133-143.
18. Popkin DR, Scali V, Ahmed MN. Cryosurgery for the treatment of cervical intraepithelial neoplasia. Am J Obstet Gynecol. 1978;130:551-554.
19. Spitzer M, Herman J, Krumholz BA, Lesser M. The fertility of women after cervical laser surgery. Obstet Gynecol. 1995;86:504-508.
20. Kyrgiou M, Koliopoulos G, Martin-Hirsch P, et al. Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis. Lancet. 2006;367:489-498.
21. Arbyn M, Kyrgiou M, Simoens C, et al. Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: meta-analysis. BMJ. 2008;337:a1284.
22. Prendiville W, Cullimore J, Norman S. Large loop excision of the transformation zone (LLETZ): a new method of management for women with cervical intraepithelial neoplasia. Br J Obstet Gynaecol. 1989;96:1054-1060.
23. Buller RE, Jones HW 3rd. Pregnancy following cervical conization. Am J Obstet Gynecol. 1982;142:506-512.
24. Mathevet P, Chemali E, Roy M, Dargent D. Long-term outcome of a randomized study comparing three techniques of conization: cold knife, laser, and LEEP. Eur J Obstet Gynecol Reprod Biol. 2003;106:214-218.
25. Sagot P, Caroit Y, Winer N, et al. Obstetrical prognosis for carbon dioxide laser conisation of the uterine cervix. Eur J Obstet Gynecol Reprod Biol. 1995;58:53-58.
26. Kristensen J, Langhoff-Roos J, Wittrup M, Bock JE. Cervical conization and preterm delivery/low birth weight: a systematic review of the literature. Acta Obstet Gynecol Scand. 1993;72:640-644.
27. Monteiro AC, Russomano FB, Camargo MJ, et al. Cervical stenosis following electrosurgical conization. Sao Paulo Med J. 2008;126:209-214.
28. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 99: management of abnormal cervical cytology and histology. Obstet Gynecol. 2008;112:1419-1444.
29. Dargent D. Treatment of dysplasias and cancers of the cervix: in defense of and illustration of the conization procedure using a cold scalpel under local anesthesia with hospitalization for a day. Rev Fr Gynecol Obstet. 1985;80:543-548.
30. Martin-Hirsch PP, Paraskevaidis E, Bryant A, et al. Surgery for cervical intraepithelial neoplasia. Cochrane Database Syst Rev. 2010;6:CD001318.
31. Moinian M, Andersch B. Does cervix conization increase the risk of complications in subsequent pregnancies? Acta Obstet Gyne-

col Scand. 1982;61:101-103.
32. Baldauf JJ, Dreyfus M, Ritter J, et al. Risk of cervical stenosis after large loop excision or laser conization. Obstet Gynecol. 1996;88:933-938.
33. Santos C, Galdos R, Alvarez M, et al. One-session management of cervical intraepithelial neoplasia: a solution for developing countries. A prospective, randomized Trial of LEEP versus laser excisional conization. Gynecol Oncol. 1996;61:11-15.
34. Plante M, Renaud MC, Roy M. Radical vaginal trachelectomy: a fertility-preserving option for young women with early stage cervical cancer. Gynecol Oncol. 2005;99(3 suppl 1):S143-S146.
35. Dargent D. Radical trachelectomy: an operation that preserves the fertility of young women with invasive cervical cancer. Bull Acad Natl Med. 2001;185:1295-1304; discussion, 1305-1306.
36. Dursun P, LeBlanc E, Nogueira MC. Radical vaginal trachelectomy (Dargent's operation): a critical review of the literature. Eur J Surg Oncol. 2007;33:933-941.
37. Alexander-Sefre F, Chee N, Spencer C, et al. Surgical morbidity associated with radical trachelectomy and radical hysterectomy. Gynecol Oncol. 2006;101:450-454.
38. Marchiole P, Benchaib M, Buenerd A, et al. Oncological safety of laparoscopic-assisted vaginal radical trachelectomy (LARVT or Dargent's operation): a comparative study with laparoscopic-assisted vaginal radical hysterectomy (LARVH). Gynecol Oncol. 2007;106:132-141.
39. Shepherd JH, Spencer C, Herod J, Ind TE. Radical vaginal trachelectomy as a fertility-sparing procedure in women with early-stage cervical cancer-cumulative pregnancy rate in a series of 123 women., BJOG. 2006;113:719-724.
40. Plante M. Vaginal radical trachelectomy: an update. Gynecol Oncol. 2008;111(2 suppl):S105-S110.
41. Jolley JA, Battista L, Wing DA. Management of pregnancy after radical trachelectomy: case reports and systematic review of the literature. Am J Perinatol. 2007;24:531-539.
42. Martin JA, Kung HC, Mathews TJ, et al. Annual summary of vital statistics. Pediatrics. 2008;121:788-801.
43. Jolley JA, Wing DA. Pregnancy management after cervical surgery. Curr Opin Obstet Gynecol. 2008;20:528-533.
44. Bernardini M, Barrett J, Seaward G, Covens A. Pregnancy outcomes in patients after radical trachelectomy. Am J Obstet Gynecol. 2003;189:1378-1382.
45. Karat C, Madhivanan P, Krupp K, et al. The clinical and microbiological correlates of premature rupture of membranes. Indian J Med Microbiol. 2006;24:283-285.
46. Khalid S, Dimitriou E, Prendiville W. Risk of premature labor after LLETZ: does size matter? Paper presented at: British Society for Colposcopy and Cervical Pathology Annual Meeting; 2009; Dublin, Ireland.
47. Himes KP, Simhan HN. Time from cervical conization to pregnancy and preterm birth. Obstet Gynecol. 2007;109:314-319.
48. Mella MT, Berghella V. Prediction of preterm birth: cervical sonography. Semin Perinatol. 2009;33:317-324.
49. Crane JM, Delaney T, Hutchens D. Transvaginal ultrasonography in the prediction of preterm birth after treatment for cervical intraepithelial neoplasia. Obstet Gynecol. 2006;107:37-44.
50. Meis PJ, Klebanoff M, Thom E, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med. 2003;348:2379-2385.
51. Berghella V, Figueroa D, Szychowski JM, et al. Vaginal Ultrasound Trial Consortium. 17-alpha-hydroxyprogesterone caproate for the prevention of preterm birth in women with prior preterm birth and a short cervical length. Am J Obstet Gynecol. 2010;202:351.e1-6.
52. Zeisler H, Joura EA, Bancher-Todesca D, et al. Prophylactic cerclage in pregnancy: effect in women with a history of conization. J Reprod Med. 1997;42:390-392.

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- Risks and benefits of gonadotropin stimulation with intrauterine insemination

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