About 68% of invasive cervical cancer cases diagnosed in the United States involve women of childbearing age. Current treatment options for young patients with cervical cancer may cause hormonal and/or structural modifications to the reproductive system that could compromise pregnancy potential. Although clinical guidelines are available to help preserve fertility in these patients, gaps in practice remain, suggesting that the fertility-sparing needs of cervical cancer survivors are not routinely met. The authors provide nurse practitioners with current evidence about fertility-sparing treatments and with counseling considerations for young cervical cancer survivors.

**Key words:** cervical cancer survivor, fertility-sparing treatment, pregnancy, infertility, conization, trachelectomy

Cervical cancer was once the leading cause of gynecologic cancer in the United States. Following introduction of the use of the Pap smear in the 1940s, the incidence of cervical cancer has declined dramatically. Because use of the Pap smear is so effective and so widespread, the diagnosis of cervical cancer, when it is found, is usually made when a woman is younger (and still fertile) and when the disease is at an earlier stage (and therefore more easily treated).

In 2014, the American Cancer Society projected that 12,360 new cases of cervical cancer would be diagnosed in the U.S.2 Approximately 68% of cervical cancer cases are diagnosed in women of childbearing age.3,4 For young women, a diagnosis of cervical cancer once meant a hysterectomy and loss of the ability to bear a child. Today, fertility-sparing treatment (FST) options exist for women with early-stage cervical cancer, as well as more advanced fertility preservation and assisted reproductive technology (ART) approaches for those who are not candidates for FST.5

Young cervical cancer survivors may not know about FST options, and thus fear that treatment for cancer may compromise their future ability to conceive.6 Survivors also tend to be anxious about pregnancy outcomes after completing cancer treatment.7,8 Evidence suggests that they will want to discuss future fertility options.
with their healthcare provider (HCP). The American Society of Clinical Oncology (ASCO) and the American Society of Reproductive Medicine have published guidelines recommending that, prior to treatment, HCPs educate patients diagnosed with cervical cancer about the treatment’s potential effects on their fertility, along with fertility-preservation options. However, many HCPs are uninformed themselves and do not routinely offer fertility-preservation counseling prior to cancer treatment. The purpose of this article is to provide HCPs with current evidence about FST for cervical cancer and with counseling recommendations for young cervical cancer survivors.

**Diagnosis and staging of cervical cancer**

A Pap smear is used to screen for cervical cancer but not to make the diagnosis. A histology report from a cervical biopsy confirms the diagnosis and type of cervical cancer. After diagnosis, a workup is done to determine disease stage (Table 1).

A clinical staging system is used for cervical cancer (rather than the surgical criteria used for most gynecologic cancers). Two different staging systems are available. The International Federation of Gynecology and Obstetrics (FIGO) staging system is based on a physical examination, diagnostic procedures, and imaging studies. Stages IA1, IA2, and IB1 are considered early stages of cervical cancer. In stages IA1 and IA2, cancer is confined to the cervix and diagnosed only microscopically. Stage IB1 describes cancer confined to the cervix with a clinically visible tumor ≤4 cm, stromal invasion <10 mm, and no lymph vascular space invasion.

**Table 1. FIGO cervical cancer clinical staging workup**

<table>
<thead>
<tr>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>History and physical examination</td>
</tr>
<tr>
<td>Chest radiograph</td>
</tr>
<tr>
<td>Complete blood count</td>
</tr>
<tr>
<td>CT or PET-CT scan</td>
</tr>
<tr>
<td>Cervical biopsy</td>
</tr>
<tr>
<td>MRI as indicated</td>
</tr>
<tr>
<td>Cone biopsy as indicated</td>
</tr>
<tr>
<td>HIV testing as indicated</td>
</tr>
<tr>
<td>Smoking cessation and counseling as indicated</td>
</tr>
<tr>
<td>Cystoscopy or proctoscopy for patients in whom bladder/bowel involvement is suspected</td>
</tr>
</tbody>
</table>

CT, computed tomography; FIGO, International Federation of Gynecology and Obstetrics; MRI, magnetic resonance imaging; PET, positron emission tomography.

**Young cervical cancer survivors may not know about fertility-sparing treatment options, and thus fear that treatment for cancer may compromise their future ability to conceive.**

American Joint Committee on Cancer created the TNM system, which is based on extent of the tumor (T), node involvement (N), and distant metastases presentation (M). Each stage in this system has substages that further describe tissue involvement (Table 2).

**Cone biopsy**

This term refers to a wedge-shaped excision of cervical tissue for both diagnostic evaluation and removal of abnormal tissue. Two methods of obtaining a cone biopsy with fertility sparing in mind are cold knife conization (CKC) and the loop electrosurgical excision procedure (LEEP).

Cone biopsy is used to treat small lesions when there is no risk of dissecting across a gross neoplasm. Given that adequate margins and correct orientation are...
obtained, CKC and LEEP are appropriate measures for cervical cancer stage IA1 without lymphovascular space invasion.\textsuperscript{5} Negligible risks exist for cervical cancer stage IA1 recurrence following this treatment.\textsuperscript{5}

Potential risks regarding future fertility following a cone biopsy include cervical stenosis and preterm delivery.\textsuperscript{18,19} Cervical stenosis occurs in 2%-3% of patients after CKC and in 3%-4% post-LEEP.\textsuperscript{19} Because of scar tissue formation that can occur after a cone biopsy, fertility may be compromised until the tissue is removed from the cervix. Long and Leeman\textsuperscript{19} reported that a history of a cone biopsy increased the odds of a preterm delivery by 2.19 (95% confidence interval, 1.93-2.49); risk correlated with the depth of the transformation zone removed. In this study, a greater risk existed for preterm delivery when a cone biopsy sample was thicker than 1.2 cm and larger than 6 cm\textsuperscript{2}. However, Bevis and Biggio\textsuperscript{18} reported that evidence for the effects of conization procedures on fertility was conflicting because of the different types of procedures performed and the varying quality of control groups.

Fanfani et al\textsuperscript{20} performed a multicenter retrospective analysis of reproductive outcomes in 23 early-stage cervical cancer survivors who had undergone conization treatment. Among 10 patients who tried to conceive, 6 achieved a spontaneous pregnancy and 4 received conception assistance via in vitro fertilization and embryo transfer (1 of whom achieved a pregnancy). In total, 70% of the young survivors achieved a pregnancy after cone biopsy treatment.

**Trachelectomy**

This fertility-sparing surgical procedure is performed to eradicate cervical cancer. In an RVT, the uterine corpus, ovaries, and Fallopian tubes are preserved, but the cervix, upper portion of the vagina, and the supporting ligaments are removed. A cerclage is placed at the location of the isthmus to close the opening of the uterus.\textsuperscript{7} RVT is an option for patients with stage IA2 or IB1 lesions <2 cm in diameter. A radical abdominal trachelectomy is used for stage IB1 lesions >2 cm and ≤4 cm, and provides a larger resection of the parametria.\textsuperscript{5}

Most women who undergo RVT are able to conceive spontaneously, but a small number will require conception assistance.\textsuperscript{21} The 5-year cumulative pregnancy rate for women trying to conceive post-RVT is 52.8%; the cervical cancer recurrence rate after the procedure continues to be low.\textsuperscript{7} Potential risks of either trachelectomy procedure with regard to future fertility include miscarriage, preterm delivery, anovulation, and isthmic stenosis.\textsuperscript{7,21}

Koh et al\textsuperscript{5} reported that, worldwide, more than 300 pregnancies have been confirmed following a trachelectomy for cervical cancer. Risk for second trimester miscarriage following a trachelectomy is 10%. However, 72% of women have carried a pregnancy to term. Park et al\textsuperscript{22} conducted a retrospective chart review of 55 young

### Table 2. Cervical cancer staging systems\textsuperscript{5,15,16}

<table>
<thead>
<tr>
<th>AJCC TNM stage</th>
<th>FIGO stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>I</td>
<td>Carcinoma confined to the cervix</td>
</tr>
<tr>
<td>T1a</td>
<td>IA</td>
<td>Microscopy-visualized invasive carcinoma with deepest invasion ≤5 mm and largest extension ≤7 mm</td>
</tr>
<tr>
<td>T1a1</td>
<td>IA1</td>
<td>Measured stromal invasion ≤3 mm in depth and largest extension ≤7 mm</td>
</tr>
<tr>
<td>T1a2</td>
<td>IA2</td>
<td>Measured stromal invasion &gt;3 mm and ≤5 mm, with largest extension ≤7 mm</td>
</tr>
<tr>
<td>T1b</td>
<td>IB</td>
<td>Clinically visualized lesion confined to the cervix uteri or preclinical cancers greater than stage T1a/IA2</td>
</tr>
<tr>
<td>T1b1</td>
<td>IB1</td>
<td>Clinically visualized lesion ≤4 cm in greatest dimension</td>
</tr>
<tr>
<td>T1b2</td>
<td>IB2</td>
<td>Clinically visualized lesion &gt;4 cm in greatest dimension</td>
</tr>
</tbody>
</table>

AJCC, American Joint Committee on Cancer; FIGO, International Federation of Gynecology and Obstetrics.
early-stage cervical cancer survivors who underwent laparoscopic abdominal trachelectomy. Ten of 18 patients attempting a pregnancy conceived; 6 of the 10 experienced preterm delivery. Overall, 55.6% of the survivors achieved a pregnancy, with 60% delivering preterm.

Fertility preservation procedures
Most women with cervical cancer at stage IB2 or greater are not candidates for FST. Radiation therapy is most often used for patients with higher stage IB disease, often called bulky disease. Radiation therapy is also used following a primary radical hysterectomy or in conjunction with chemotherapy in advanced disease. Radiation that includes the ovaries can damage oocyte quality and sex hormone production. Chemotherapy is not used in patients with milder forms of cervical cancer who are considering FST options.

Women planning to undergo radiation still have fertility preservation options, including the ART procedures of oocyte or embryo cryopreservation prior to cancer treatment.23 Cryopreservation of unfertilized oocytes, as opposed to embryos, may be considered for patients who do not have a male partner, do not wish to use donor sperm, or have religious or ethical reasons for avoiding embryo freezing. Because oocytes are highly sensitive to radiation injury, a procedure called oophoropexy (ovarian transposition) may be used. With oophoropexy, ovaries are sutured to the posterior uterus to protect them during pelvic radiation.

Before or after cancer treatment, survivors may benefit from ovarian stimulation medications that help promote follicular development. However, guidelines from both the American Congress of Obstetricians and Gynecologists and ASCO indicate insufficient evidence regarding the effectiveness of gonadotropin-releasing hormone analogs to suppress and protect ovarian function during cytotoxic treatment.24

Counseling before treatment
These counseling recommendations concerning fertility preservation were issued by ASCO: (1) Assume that patients with cancer want to discuss fertility preservation; address the possibility of infertility before cancer treatment starts and work with an interdisciplinary team to formulate a plan and make appropriate referrals; (2) Present oocyte and embryo cryopreservation as established fertility preservation methods; (3) Discuss the option of oophoropexy when pelvic radiation will be performed; (4) Inform patients of their individual risk for infertility, based on disease stage and treatment, as high, medium, low, or nonexistent; and (5) Inform patients about the use of conservative gynecologic surgery and radiation options.11

Several organizations and advocacy groups are available for young cervical cancer survivors with fertility concerns both before and after treatment (Table 3). ASCO created a video that can educate young pa-

Table 3. Resources

- American Society of Clinical Oncology: www.asco.org/
- National Cervical Cancer Coalition: www.nccc-online.org/
- Resolve: The National Infertility Association: www.resolve.org/
- Save My Fertility: http://www.savemyfertility.org/
- The Oncofertility Consortium: http://oncofertility.northwestern.edu/

Inform patients of their individual risk for infertility, based on disease stage and treatment, as high, medium, low, or nonexistent.

[VIEW: Fertility preservation for young women with cancer]

www.NPWomensHealthcare.com

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Table 4. Physical and psychological problems involving sexual function

<table>
<thead>
<tr>
<th>Physical problems</th>
<th>Psychosocial problems</th>
<th>Drug classes that can affect libido</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adhesions</td>
<td>Anxiety</td>
<td>Antidepressants</td>
</tr>
<tr>
<td>Changes in energy level</td>
<td>Arousal difficulties</td>
<td>Anxiolytics</td>
</tr>
<tr>
<td>Damage to nerves</td>
<td>Changes in relationships</td>
<td>Opioids</td>
</tr>
<tr>
<td>Decreased intimacy</td>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td>Decreased libido</td>
<td>Fear (of change)</td>
<td></td>
</tr>
<tr>
<td>Decreased vaginal elasticity</td>
<td>Fear (or recurrence)</td>
<td></td>
</tr>
<tr>
<td>Difficulty with conception</td>
<td>Lack of desire</td>
<td></td>
</tr>
<tr>
<td>Difficulty with lubrication</td>
<td>Reproductive concerns</td>
<td></td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>Sexual worry</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrosis</td>
<td></td>
<td></td>
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<tr>
<td>Inflammation</td>
<td></td>
<td></td>
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<tr>
<td>Miscarriage</td>
<td></td>
<td></td>
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<tr>
<td>Preterm delivery</td>
<td></td>
<td></td>
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<tr>
<td>Radiation</td>
<td></td>
<td></td>
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<tr>
<td>Risk of infertility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scarring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
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<tr>
<td>Vaginal stenosis</td>
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<td></td>
</tr>
</tbody>
</table>

Even if a woman succeeds in achieving pregnancy through ART, the process is often fraught with anxiety. Young female cancer survivors have reported that they have a hopeful yet worried outlook on fertility and motherhood. This worry is especially true for cervical cancer survivors who have had trachelectomy surgery, as reported by Lloyd et al, wherein several participants described how they were fearful during pregnancy and attempted to be “model” pregnant women who followed every recommendation to reduce risks associated with preterm labor and miscarriage.

Consultations with specialists in reproductive endocrinology and/or high-risk obstetrics may be helpful. Pregnancy loss after infer-
tility treatment can be devastating to these women, who view their pregnancy as “precious” and a “miracle,” and can have a profound impact on their psychological well-being. HCPs should promptly refer these cancer survivors to mental health counselors who specialize in infertility and pregnancy loss.

Conclusion
Sixty-eight percent of cervical cancer cases diagnosed in the U.S. involve reproductive-aged women. Many of these women desire future pregnancies and want to discuss treatment options and future fertility. An interdisciplinary care approach for these women is necessary, with an emphasis placed on both successful cancer treatment and fertility preservation. FST options are available for women with early-stage cancer up to IB1. Fertility preservation procedures are available for women who are not candidates for FST. National guidelines are available regarding treatment and counseling for reproductive-age women with cervical cancer. The role of HCPs such as women’s health nurse practitioners is to educate young cervical cancer patients and survivors about their treatment options, manage pre- and post-treatment care, and provide referrals to specialists as needed.

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References
22. Park JY, Kim DY, Suh DS, et al. (continued on page 49)
nician/Clinician II at Planned Parenthood Mar Monte in San Jose, California. Victoria S. Tueros is a Family Nurse Practitioner in the Women’s Clinic at Family Health Centers Logan Heights in San Diego, California. The authors state that they do not have a financial interest in or other relationship with any commercial product named in this article.

References

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Web resources
A. https://www.youtube.com/watch?v=N51GrR8QXQA
B. www.facit.org/FACITOrg/Questionnaires