Chapter 2■ Stage 0 disease

Overview

In clinical staging (Japan Society of Obstetrics and Gynecology, 1997) 'stage 0 is defined as 'carcinoma in situ.' However, the 1993 International Federation of Gynecology and Obstetrics (FIGO) staging includes carcinoma in situ and CIN3 in stage 0. Cervical intraepithelial neoplasia (CIN) is a name derived from the concept of a continuum of lesions from dysplasia to carcinoma in situ. CIN is divided into 3 levels by the degree of dysplasia: CIN1 mild dysplasia, CIN2 moderate dysplasia, and CIN3 severe dysplasia to carcinoma in situ.

Cervical cancer is often detected early through screening programs. The number of patients with stage 0 disease is also on the rise, and stage 0 accounted for 46% of all Japanese cervical cancer patients in 2003.[1]

Human papillomavirus (HPV) infection is considered to be associated with the development of cervical cancer. In recent years, HPV infection has been spreading due to changes in sexual behavior in younger age groups. In 2004, the Health and Medical Service Law for the Aged underwent a partial revision, and the target for cervical screening was lowered to include women aged 20 and over. It is therefore likely that cervical cancer will be detected in more patients in younger age groups. In recent years, women have been tending to marry later and have children later in their lives. This trend means that more patients with cervical cancer will be likely to request uterine preservation. Data published by the Japan Society of Obstetrics and Gynecology shows that 33% of stage 0 patients underwent cervical cone biopsy in 1990[2], and 73% in 2003.[1]

Cervical cone biopsy is the definitive treatment for patients with stage 0 disease, with no evidence of invasion or residual lesions in the preserved uterus following cervical cone biopsy. However, total hysterectomy should be considered for patients who do not desire fertility preservation.

For CIN, treatments that have been trialed include cervical cone biopsy, hysterectomy, cryotherapy, and laser ablation. Cervical cone biopsy enables histopathological examination of the resected specimen, whereas cryotherapy and laser ablation have the disadvantage of not allowing histological examination of the frozen or vaporized area. Although small in number, there are some patients with microinvasive or invasive cancer among those preoperatively determined to have carcinoma in situ. Cervical cone biopsy is therefore recommended for stage 0 disease because this method allows a tissue diagnosis.

Cervical cone biopsy procedures traditionally involved the use of a scalpel, but more recently laser, high frequency current, and ultrasound have been used widely. Lasers used include the CO_2 and YAG types. Methods using high frequency current include LEEP (loop electrosurgical excision procedure) and the Shimodaira method. A variety of electrodes are used, including loop-shaped, triangular, needle-shaped, and spherical electrodes. Each clinician should become well versed in various methods, and equipment types, and select a specific method of cervical cone biopsy.

Treatments for squamous cell carcinoma in situ and adenocarcinoma in situ differ slightly, and in this chapter we will discuss treatments for squamous cell carcinoma in situ. Treatments for adenocarcinoma in situ will be discussed in Chapter 8.

References

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CQ01
What is the optimal surgical procedure for stage 0 disease?

Recommendations

(1) Cervical cone biopsy is recommended (Grade B).
(2) Total hysterectomy should be considered for patients who do not desire fertility preservation (Grade C).

Background and Objectives

We examined the optimal treatments for stage 0 disease.

Explanation

Lymphadenectomy is considered unnecessary for carcinoma in situ due to its histological characteristics. Conventionally, total hysterectomy has been the standard surgical procedure. However, cervical cone biopsy is frequently selected as fertility preserving treatment due to the recent increase in young patients with carcinoma in situ.[1-3] According to the report of the Gynecologic Oncology Committee of the Japan Society of Obstetrics and Gynecology, cervical cone biopsy was the treatment for stage 0 disease in 33% of patients in 1990,[4] increasing to 73% in 2003.[5] Total hysterectomy should be considered for for elderly patients and patients who do not desire fertility preservation. Although small in number, there are some patients with microinvasive or invasive cancer among those preoperatively diagnosed with severe dysplasia or carcinoma in situ. It is therefore appropriate to perform cervical cone biopsy and then determine whether a hysterectomy is necessary.[2,3,6,7]

Cervical cone biopsy procedures were traditionally performed using a scalpel (cold knife) until lasers came into use in the 1990s.[8-11] In recent years, high frequency current and ultrasound are also used widely. Lasers used include the CO2 and YAG types. Methods using high frequency current include LEEP (loop electrosurgical excision procedure) and the Shimodaira method. A variety of electrodes are used, including loop-shaped, triangular, needle-shaped, and spherical electrodes. Each clinician should become well versed in various methods, and equipment types, and select a specific method of cervical cone biopsy.

Cervical cone biopsy using a cold knife does not cause thermal tissue degeneration, and therefore has the advantage of enabling accurate pathological diagnosis.[12] This procedure has been reported to have similar therapeutic outcomes to laser cervical cone biopsy and LEEP.[13] However, caution is required if suturing is performed, since residual cancer cells on the uterine side can readily become embedded in the cervical canal. As with cold knife cone biopsy, laser cone biopsy can excise a specimen in one piece with sufficient depth. Laser cone biopsy is therefore indicated for the diagnosis and treatment of all cervical intraepithelial neoplasia (CIN) types regardless of the location of the lesion.[1-3,6-10,14-16] Reported cure rates approach 100%.[2,3,6,7,16] In contrast, since the depth of the excised specimen is often insufficient with LEEP, there is

a high risk of leaving behind residual cancer if the lesion extends deeply into the cervical canal. In stage 0, therapeutic outcomes with LEEP are reported to be inferior to those obtained with laser cone biopsy.[17] The application of LEEP should be limited to patients with lesions confined to the vaginal portion of the cervix. Since LEEP can be performed relatively easily, and allows some degree of histological diagnosis, it has potential as a useful conservative treatment for CIN if the indications can be thoroughly defined.[17-19] Through endocervical curettage at preoperative diagnosis or cone biopsy, some studies found that residual lesions on the uterine side and the presence of unexpected invasive cancer can be predicted for the following types of patient subgroups. These were: lesions that could not be fully confirmed at colposcopy, suspected endocervical lesions, and results of diagnostic cytology worse than those from diagnostic biopsy.[20-23]

Since specimens cannot be obtained by ablation or cryotherapy, high diagnostic accuracy is demanded from preoperative cytological diagnosis, colposcopy, or histological diagnosis. Ablation and cryotherapy are mainly indicated for lesions which are entirely visible using colposcopy, or for moderate to severe dysplasia. In recent years, ablation and cryotherapy has been reported to be particularly useful for CIN cases with visible lesions that can be fully evaluated by colposcopy.[18,24,25] Although small in number, there are some patients with microinvasive or invasive cancer among those preoperatively diagnosed with severe dysplasia or carcinoma in situ. Caution is therefore required when performing conservative treatments such as laser ablation and cryotherapy, since a tissue diagnosis cannot be obtained with these methods.[2,3,6,7,14,15]

Photodynamic therapy (PDT) is a conservative treatment using a low-output excimer dye laser and an oncotropic photosensitive substance such as porfimer sodium.[26-28] Possible adverse reactions include severe photosensitivity, adversing affecting daily life. The application of PDT is difficult, and requires special equipment and facilities, so it is widely used as standard therapy.

Recently, the effects of cone biopsy on subsequent pregnancy and delivery have attracted considerable attention.[29,30] Kyrgiou et al.[29] conducted a meta-analysis of 27 studies on the obstetric prognosis following conservative treatment for CIN and early invasive cancer. They found that cold knife, LEEP, and laser cone biopsy significantly increased the risk of premature birth, low birth weight, and Cesarean section. In the future, before cervical cone biopsy is performed in patients who desire to have a child, it will be necessary to thoroughly inform the patients of the possible risks and obtain their informed consent.

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CQ02
What treatments are recommended for recurrence following conservative treatment?

Recommendations

(1) For recurrence following laser cone biopsy or LEEP, the same procedure should be repeated, or total hysterectomy considered, depending on the patient (Grade B).
(2) For recurrence following laser ablation or cryotherapy, cone biopsy or total hysterectomy is recommended (Grade B).

Background and Objectives

We examined treatments for recurrence following conservative treatment.

Explanation

Patients with positive resection margins had a recurrence rate of 9-16% following LEEP or laser cone biopsy, whereas those with negative resection margins had a recurrence rate of 2-4%.[1,2] Even for cases with positive resection margins, spontaneous resolution was reported during the follow-up period in 67% of patients in whom the residual lesion on the uterine side was ≤CIN 2.[3] In any case, careful follow-up is needed for patients with positive resection margins. Cone biopsy should be repeated in patients with positive resection margins or recurrence, and hysterectomy should be considered if invasive cancer is suspected.[4-7] When ablation of the resection surface was performed in addition to cone biopsy, prevention of residual lesions on the uterine side and recurrence was reported.[6-8]

Since laser ablation and cryotherapy do not provide tissue specimens, a definitive diagnosis cannot be made with these methods. Although small in number, there are some patients with carcinoma in situ or invasive cancer among those preoperatively diagnosed with cervical intraepithelial neoplasia (CIN).[4-7] There are also a small proportion of patients in whom invasive cancer is detected in the course of long-term follow-up. It is therefore recommended that a definite tissue diagnosis be obtained by performing cervical cone biopsy or hysterectomy for recurrences in stage 0 or greater.[9]

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