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An Overview on Cervical Intraepithelial Neoplasia (CIN)

Aml Abd ElAziz Elsayed Nouh [1], Mona Mostafa Ahmed[2], Aziza Mostafa Abd Elhamid[1], Reham Essam Kamel[3] , Mohamed A. Helmy[1]

[1]Obstetrics & Gynecology Department, Faculty of Medicine, Zagazig University, Egypt

[2]Pathology Department, Faculty of Medicine, Zagazig University, Egypt

[3]Dermatology and Venereology Department, Faculty of Medicine, Zagazig University, Egypt

***Corresponding author:** Aziza Mostafa Abd Elhamid

Abstract

Background: Cervical intraepithelial neoplasia (CIN) represents premalignant changes in the squamous epithelium of the cervix and is strongly associated with persistent infection with high-risk human papillomavirus (HPV), particularly types 16 and 18. CIN is histologically classified into three grades (CIN 1, CIN 2, and CIN 3) based on the extent of epithelial dysplasia. While low-grade lesions (CIN 1) often regress spontaneously, high-grade lesions (CIN 2 and CIN 3) carry a significant risk of progression to invasive cervical carcinoma if left untreated. Early detection through cervical cytology (Pap smear), HPV testing, and colposcopic evaluation has markedly reduced the incidence and mortality of cervical cancer worldwide. Management strategies depend on lesion grade, patient age, reproductive plans, and associated risk factors, and range from observation to ablative or excisional procedures such as loop electrosurgical excision procedure (LEEP) or cold knife conization.

Keywords: Cervical intraepithelial neoplasia; CIN; Human papillomavirus; Cervical dysplasia; Pap smear; Colposcopy; LEEP; Cervical cancer prevention.

Introduction

Cervical intraepithelial neoplasia (CIN) is a premalignant condition of the cervix, also referred to as cervical dysplasia or squamous intraepithelial lesions (SIL). Previously, premalignant cervical changes were classified as mild, moderate, and severe dysplasia. Although these terms are still used in some settings, they have largely been replaced by the term cervical intraepithelial neoplasia (CIN) to describe histological changes of the uterine cervix. More recently, there has been a shift toward the use of squamous intraepithelial lesion (SIL) terminology, particularly in cytological reporting(1).

Incidence

The incidence of cervical intraepithelial neoplasia (CIN) varies according to age, screening practices, and HPV vaccination coverage. Population-based surveillance data from the United States indicate that low-grade lesions (CIN 1) are relatively common among screened women, while high-grade lesions (CIN 2 and CIN 3) occur less frequently and show marked age-specific variation. High-grade CIN is most commonly diagnosed in women aged 25–35 years, reflecting the peak prevalence of persistent high-risk HPV infection, whereas invasive cervical cancer is more frequently diagnosed after the age of 40, typically following a latency period of 8–15 years after the development of high-grade precursor lesions.

Recent data demonstrate a substantial decline in the incidence of CIN 2+ lesions in the United States, particularly among younger women, largely attributable to the widespread implementation of HPV vaccination and improved screening strategies. Surveillance reports from the Centers for Disease Control and Prevention (CDC) show reductions of up to 70–80% in CIN 2+ incidence among women aged 20–24 years over the past decade.

In low- and middle-income countries, reported CIN prevalence varies widely and is strongly influenced by access to screening programs. Studies from sub-Saharan Africa, including Nigeria, have reported a mean age of CIN diagnosis in the late 30s; however, the apparently lower prevalence of CIN in these settings is largely attributable to under-screening and under-diagnosis rather than a true reduction in disease burden.

Given that CIN is a premalignant precursor of cervical cancer, understanding the global burden of cervical cancer is essential. According to the World Health Organization (WHO) and GLOBOCAN 2020 data, cervical cancer is currently the fourth most common cancer among women worldwide, with an estimated 604,000 new cases and 342,000 deaths annually. Approximately 90% of cases and deaths occur in low- and middle-income countries, reflecting disparities in HPV vaccination, screening, and access to treatment services.

Since cervical intraepithelial neoplasia (CIN) is a premalignant precursor of cervical cancer, understanding the global incidence and prevalence of cervical cancer is essential. Cervical cancer remains a major public health problem and is currently the fourth most common cancer among women worldwide. According to recent World Health Organization (WHO) and GLOBOCAN data, an estimated 604,000 new cases of cervical cancer and approximately 342,000 deaths occur globally each year. Nearly 90% of cervical cancer cases and deaths occur in low- and middle-income countries, largely due to limited access to effective screening, vaccination, and treatment services .

Predisposing Factors

Risk factors for preinvasive cervical lesions are multifactorial and include sexual behavior, demographic factors, lifestyle factors, and biological influences. The most important risk factor is infection with human papillomavirus (HPV), particularly high-risk types such as HPV 16 and 18, which are strongly associated with the development of cervical precancerous lesions (1).

- The population distribution of cervical intraepithelial neoplasia resembles the epidemiology of a sexually transmitted infection.
- Multiple sexual partners.
- Early age at first sexual intercourse.
- A male partner with multiple previous or current female sexual partners is an important risk factor.

Etiology

Human papillomavirus (HPV) infection of the cervix is a sexually transmitted infection and a major risk factor for the development of cervical intraepithelial neoplasia. However, only a small proportion of infected women progress to severe CIN or invasive cervical cancer. Disease progression depends on several factors, the most important of which is the HPV genotype responsible for the infection (3).

Pathophysiology

Cervical intraepithelial neoplasia results from HPV infection of cervical epithelial cells. In many cases, particularly in young women, these changes regress spontaneously due to an effective immune response and rapid epithelial turnover. Approximately 60% of CIN 1 lesions regress within one year (1).

Women with CIN 2 and CIN 3 are at a significantly higher risk of developing invasive cervical cancer, although progression typically occurs over several years. Therefore, treatment is generally recommended for CIN 2/3 lesions, with exceptions for women aged 20–24 years and pregnant women.

Because a substantial proportion of low-grade squamous intraepithelial lesions (LSIL) detected on Pap smear are associated with underlying CIN 2 or CIN 3, colposcopy and biopsy are usually required. Similarly, older women with atypical squamous cells of undetermined significance (ASC-US) and positive high-risk HPV testing require further evaluation. Cytology serves as a screening tool, whereas histological examination of cervical biopsy specimens establishes the definitive diagnosis(4).

Clinical Presentation of Preinvasive Lesions

CIN and squamous intraepithelial lesions are usually asymptomatic and not visible on gross examination. Cervical cytology can detect these lesions, which can then be visualized and characterized using colposcopy. When symptoms are present, they may include abnormal vaginal bleeding, pelvic pain, dyspareunia, or visible lesions on the exocervix (5).

Persistent HPV infection may also manifest as exophytic genital warts, which can occur at sites of direct epithelial contact, including the external and internal lower genital tract and, less commonly, the head and neck region (6).

Histopathology

The characteristic histopathological feature of HPV infection is koilocytosis, defined by perinuclear clearing (halo formation) and enlarged, irregular nuclei. The grade of CIN is determined by the proportion of the cervical epithelium involved by dysplastic cells. CIN 1 involves the lower one-third of the epithelium, whereas CIN 2 and CIN 3 involve up to two-thirds or the full thickness of the epithelium. Progression to invasive cancer occurs when dysplastic cells breach the basement membrane (2).

History and Physical Examination

In most cases, dysplastic cervical lesions are not visible on naked-eye examination, and abnormalities are detected through Pap smear screening. Some lesions may appear as exophytic or plaque-like growths on the cervix. HPV infection may also cause anogenital warts, prompting further evaluation for associated cervical abnormalities (7).

Association of HPV with CIN

Human papillomaviruses (HPV) belong to the family *Papillomaviridae*. They are epitheliotropic viruses that promote cellular proliferation, leading to benign papillomatous lesions of the genital tract, upper respiratory tract, digestive tract, and skin. More than 100 HPV types have been identified, approximately 30 of which infect the female genital tract (7).

Low-risk HPV types, such as HPV 6 and 11, are commonly associated with low-grade CIN and exophytic anogenital warts and have a low risk of malignant progression. In contrast, high-risk HPV types, including HPV 16, 18, and 33, are frequently detected in CIN 2 and CIN 3 lesions and are strongly associated with invasive cervical cancer (7).

Viral DNA Integration

Integration of high-risk HPV DNA, particularly HPV 16 and 18, into the host genome is a consistent finding in invasive cervical cancer and represents strong evidence of their oncogenic role. HPV DNA is detected in approximately 95% of invasive cervical cancers. However, HPV infection alone is insufficient for malignant transformation. Additional factors such as immune suppression, persistent infection, smoking, hormonal influences, and genetic alterations contribute to carcinogenesis (8).

Grading of CIN

- **CIN 1 (Low-grade):** Mild atypia confined to the lower one-third of the epithelium; koilocytotic changes are common, and spontaneous regression is frequent.
- **CIN 2 (High-grade):** Moderate atypia involving up to two-thirds of the epithelial thickness with partial maturation.
- **CIN 3 (High-grade):** Severe atypia involving more than two-thirds or the full thickness of the epithelium, including carcinoma in situ (9).

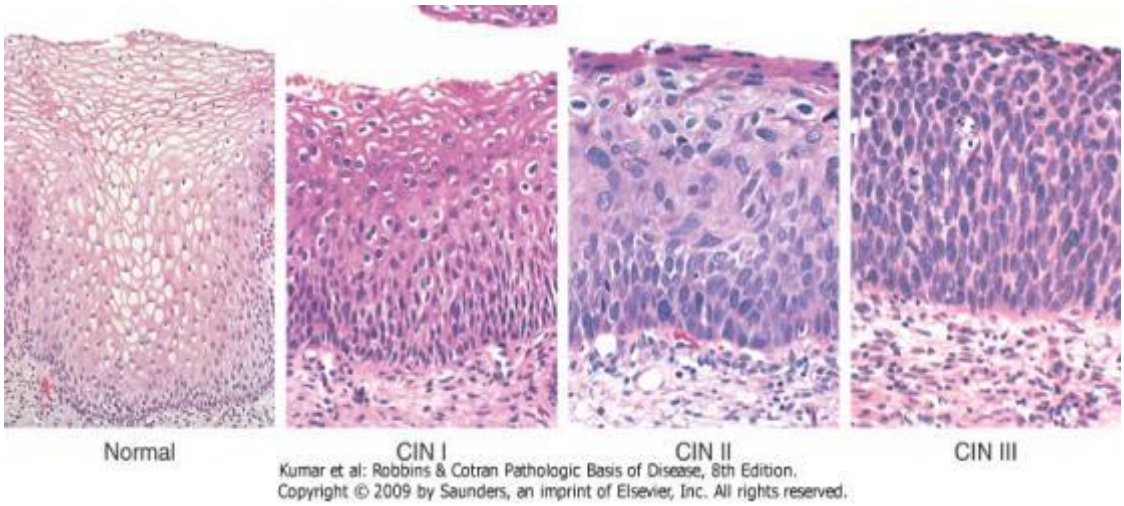


Figure (1): Normal cervix and CIN grades.

Screening of Pre-Invasive Disease of the Cervix

The primary purpose of cancer screening is to reduce mortality. Screening programs should aim to detect progressive cases during the detectable preclinical phase (10).

The ultimate indicator of screening effectiveness is a reduction in mortality. This should be demonstrated at the population level through randomized screening trials. Routine screening programs should be properly implemented and monitored (11).

According to the latest guidelines of the American Cancer Society (2023):

- Cervical cancer screening should begin at age 25 years for individuals at average risk.
- Women younger than 25 years should not be screened with either cytology (Pap test) or HPV testing.
- Women aged 25–65 years should undergo primary HPV testing every 5 years as the preferred screening strategy.
- If primary HPV testing is not available, the following acceptable alternatives may be used:
    - Co-testing (Pap test plus HPV testing) every 5 years, or
    - Cytology (Pap test) alone every 3 years.
- Annual Pap testing is not recommended, as it does not provide additional benefit and increases the risk of false-positive results.
- False-positive screening results may lead to unnecessary diagnostic procedures and treatments, including colposcopy and excisional procedures.
- The goal of population-based cervical cancer screening is to maximize early detection of clinically significant disease while minimizing overdiagnosis and overtreatment.
- Women who have undergone a total hysterectomy (with removal of the cervix) for benign disease and have no history of cervical cancer or high-grade precancerous lesions (CIN2 or higher) should not undergo cervical cancer screening.
- Women who have received HPV vaccination should continue cervical cancer screening according to age-appropriate ACS recommendations, as vaccination does not eliminate the need for screening.(12)

Pap Smear

The Pap smear evaluates cervical cells for abnormalities and is primarily a screening test. In women aged 21–29 years, it is recommended every three years. Annual screening is not recommended, as it does not significantly reduce cervical cancer mortality compared with screening at 2- or 3-year intervals (13).

The Pap smear should not be performed during menstruation. Care should be taken not to touch the exocervix when inserting the vaginal speculum to avoid contamination of the specimen. Although screening is generally avoided during menstruation, evaluation should not be delayed in cases of abnormal bleeding (e.g., cervicorrhagia or metrorrhagia) or abnormal vaginal discharge, as these may indicate underlying cervical pathology. The referral form should include the date of the last menstrual period because cervical epithelial appearance varies throughout the menstrual cycle (14).

The Bethesda Classification System

The Bethesda system is used to report cervical cytology results:

1. Negative for Intraepithelial Lesion or Malignancy (NILM)

- Adequate squamous cells with no evidence of intraepithelial lesion or malignancy, including reactive cellular changes.

2. Atypical Squamous Cells

- Cytologic changes suggestive of a squamous intraepithelial lesion but insufficient for a definitive diagnosis.

Subcategories:

- **ASC-US (Atypical Squamous Cells of Undetermined Significance)** Nuclear enlargement (2.5–3 times normal), minimal hyperchromasia, mildly irregular nuclear contours, or poorly formed cytoplasmic halos.
- **ASC-H (Atypical Squamous Cells—cannot exclude HSIL)** Scant atypical cells with features suggestive of HSIL.

3. Low-Grade Squamous Intraepithelial Lesion (LSIL)

- Corresponds to HPV-related changes and CIN 1.
- Nuclear enlargement, hyperchromasia, and mild atypia.

4. High-Grade Squamous Intraepithelial Lesion (HSIL)

- Corresponds to CIN 2 and CIN 3.
- Smaller cells with high nuclear-to-cytoplasmic (N:C) ratio, hyperchromasia, and irregular nuclear contours.

5. Squamous Cell Carcinoma

- Marked nuclear atypia, irregular nuclear membranes, coarse chromatin, tumor diathesis, and keratinization in keratinizing tumors.

Glandular Cell Abnormalities

- Atypical glandular cells (AGC)
- Atypical glandular cells, favor neoplastic
- Endocervical adenocarcinoma in situ (AIS)
- Adenocarcinoma (endocervical, endometrial, or extrauterine) (15)

Colposcopy

Principles of Colposcopy

Colposcopy is a diagnostic procedure that enables examination of the cervix and vagina using magnification (×4 to ×30) and a high-intensity light source. The examination involves sequential application of normal saline,3- 5% acetic acid, and Lugol's iodine. Disease categorization is based on integrated colposcopic findings. If abnormalities are detected, directed biopsy from the most suspicious area is required to confirm or exclude high-grade premalignant or malignant lesions (16).

IFCPC 2011 Nomenclature

The International Federation for Cervical Pathology and Colposcopy (IFCPC) introduced updated terminology in 2011 to standardize colposcopic reporting and improve reproducibility.

The examination begins with general assessment of:

- Adequacy of visualization
- Visibility of the squamocolumnar junction
- Type of transformation zone (TZ)

Findings are categorized as:

- Normal
- Abnormal
- Suspicious for invasion

Abnormal findings are further classified into:

- **Grade 1 (Minor changes):** suggestive of low-grade lesions
- **Grade 2 (Major changes):** suggestive of high-grade lesions
- **Nonspecific findings:** including leukoplakia and post-iodine changes

The miscellaneous category includes findings such as cervical polyps and condyloma(17).

Table (1): IFCPC 2011 nomenclature (**16**).

General assessment	• Adequate/inadequate for the reason… (i.e.: cervix obscured by inflammation, bleeding, and scar) • Squamocolumnar junction visibility: Completely visible, partially visible, not visible • Transformation zone types 1,2,3
Normal colposcopic findings	Original squamous epithelium: • Mature • Atrophic Columnar epithelium • Ectopy Metaplastic squamous epithelium • Nabothian cysts • Crypt (gland) openings

		Deciduosis in pregnancy	
Abnormal colposcopic findings	**General principle**	Location of the lesion: Inside or outside the T-zone Location of the lesion by clock position Size of the lesion: • Number of cervical quadrants the lesion covers • Size of the lesion in percentage of cervix	
	Grade 1 (Minor)	Thin AW epithelium Irregular, geographic border	Fine mosaic Fine punctuation
	Grade 2 (Major)	Dense acetowhite epithelium Rapid appearance of acetowhitening, cuffed crypt (gland) openings	Coarse mosaic Coarse punctuation Sharp border Inner border sign Ridge sign
	Non specific	Leukoplakia (keratosis, hyperkeratosis), erosion Lugol's staining (Schiller's test): Stained/non-stained	
Suspicious for invasion		Atypical vessels Additional signs: Fragile vessels, irregular surface, Exophytic lesion, Necrosis, Ulceration (necrotic), tumor/gross neoplasm	
Miscellaneous finding		Congenital transformation zone Condyloma Polyp (ectocervical/endocervical) Inflammation	Stenosis Congenital anomaly Post-treatment consequence Endometriosis

Colposcopic Scoring System for Grading Cervical Lesions:

To improve the predictive value of colposcopy and make the diagnosis more objective, the Swede scoring has been introduced. Swede score assigns a score of 0–2 for five different parameters listed in Table 4. A total score of less than 5 reasonably excludes high-grade lesions and biopsy may be avoided. A score of 5 to 7 is observed in low-grade or high-grade lesions and a biopsy is indicated to confirm the diagnosis. A Swede score exceeding 7 indicates the presence of high-grade lesion or even invasive cancer and if facilities are available, these lesions may be directly taken up for treatment (See and Treat) in the same sitting (**16**).

Table (2): Swede score (**16**).

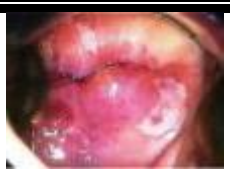
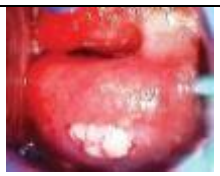
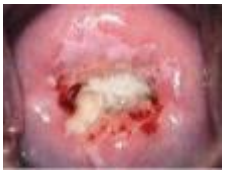
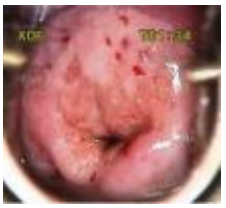
Swede scores	**0**	**1**	**2**
Aceto uptake	Zero or transparent	Thin, milky	Distinct, stearin-like
Margin and surface	Zero or diffuse	Sharp but irregular, jagged, geographical, satellites	Sharp and even, difference in surface levels including "cuffing"

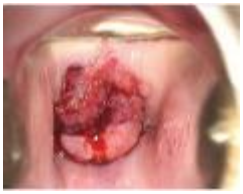
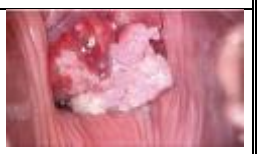
Vessels	Fine, regular	Absent	Coarse or atypical vessels
Lesion size	<5 mm	5–15 mm or spanning 2 quadrants	>15 mm or spanning 3–4 quadrants or endocervically undefined
Iodine staining	Brown	Faintly or patchy yellow	Distinct yellow

Interpretation of colposcopy findings:

A provisional colposcopy diagnosis is arrived at after completion of documentation of colposcopy findings using the IFCPC nomenclature and calculation of Swede score. (Table 3) shows colposcopy images of various lesions detected on colposcopy (**16**).

Table (3): Salient features of various lesions detected on colposcopy (**16**)

Lesion type	Salient features	Colposcopy image
Leukoplakia	• White patch with shiny, waxy surface • Sharp, raised margin	
Condyloma	• Single or multiple bright white distinct, irregular lesions • Surface irregularity (with pitted or spiky appearance)	
Condyloma/ subclinical papillomavirus infection (SPI)	• Thin/milky acetowhite patches • Irregular, geographical margin • Multiple satellite lesions	
Low-grade squamous intraepithelial lesion	• Thin acetowhite epithelium • Irregular, geographical border • Fine mosaic • Fine punctuation	
High-grade squamous intraepithelial lesion	• Dense acetowhite epithelium • Cuffed crypt (gland) openings • Coarse mosaic • Coarse punctuation • Sharp border • Inner border sign • Ridge sign	

Invasive carcinoma	•Dense acetowhite area with/without erosion • Surface irregularity • Vascular abnormalities – coarse mosaics/ coarse punctations/atypical blood vessels •Exophytic/ulcerative growth	
Adenocarcinoma	• Multiple dense acetowhite areas on columnar epithelium (grated coconut appearance) •Atypical blood vessels	

Accuracy of colposcopy:

Colposcopy is inherently subjective, and its accuracy largely depends on the quality of training and the expertise of the colposcopist in recognizing cervical abnormalities. The reported sensitivity and specificity of colposcopy vary considerably across studies.

In a meta-analysis evaluating the performance of colposcopy, Mitchell et al. (1998) reported that when a normal diagnosis was used as the threshold and compared with all other cervical abnormalities (atypia, low-grade SIL, high-grade SIL, and cancer), the average sensitivity and specificity were 96% and 48%, respectively. When the threshold was shifted to distinguish normal cervix and low-grade SIL from high-grade SIL and cancer, specificity improved to 69%, with a slight reduction in sensitivity to 85%.

Colposcopic diagnosis correlates relatively well with high-grade abnormalities, with reported sensitivities ranging from 85% to 94% for the detection of cervical precancer and cancer. However, due to limited reproducibility and relatively low specificity (approximately 50%), colposcopy is less reliable in women with minor cytological abnormalities (18).

Women with negative colposcopic findings may still be at risk of subsequently developing high-grade disease, suggesting the possibility of missed lesions. In the Atypical Squamous Cells of Undetermined Significance/Low-Grade Squamous Intraepithelial Lesion Triage Study (ASC-US/LSIL Triage Study, ALTS), the sensitivity of the initial colposcopy for predicting the development of CIN 3 over a two-year follow-up period was only 53% (16).

Most studies assessing the accuracy of colposcopy are conducted in settings where referrals are based on cytological abnormalities. This may facilitate colposcopic assessment, as the cytology results provide an indication of the expected lesion grade. Colposcopic evaluation may be more challenging when referrals are based solely on positive visual inspection with acetic acid (VIA) or positive HPV testing, where cytological guidance is unavailable.

In a population-based study conducted in Eastern India evaluating colposcopy among women with positive VIA and/or HPV tests, the sensitivity and specificity for detecting HSIL or worse (HSIL+) lesions were 84.8% and 66.1%, respectively. However, colposcopy underestimated disease severity in 52.6% of women with biopsy-confirmed HSIL. Other studies have similarly demonstrated low agreement between colposcopic impression and histological diagnosis (19).

Conization

Conization is an invasive diagnostic and therapeutic procedure that can be performed using a cold knife (cold knife conization, CKC), electrocautery (LEEP/LLETZ), laser, or other advanced surgical techniques.

Cold knife conization provides an adequate specimen for histopathological evaluation and allows precise margin assessment. Although it may be performed under general or local anesthesia, it is associated with a higher complication rate compared with other excisional methods (20).

The patient is placed in the lithotomy position, and a vaginal speculum is inserted. Colposcopic guidance and/or Lugol's iodine may be used to identify the lesion. Hemostatic sutures may be placed at the 3 and 9 o'clock positions to minimize bleeding. In selected cases, vasopressors may be injected to reduce intraoperative bleeding, provided there are no contraindications (e.g., hypertension). A circumferential incision is then made to an appropriate depth, the cone specimen is excised, and cervical reconstruction may be performed using the Sturmdorf suture technique (21).

Historically, cold knife conization was the standard technique. With advancements in surgical technology, electrosurgical excision (LEEP/LLETZ), laser conization, and other energy-based devices have become widely used. Laser conization is relatively costly and time-consuming, and both laser and LEEP may produce thermal artifacts that can complicate histological margin assessment.

A meta-analysis demonstrated that LEEP/LLETZ is comparable to CKC in terms of recurrence rate, positive surgical margins, residual disease, secondary hemorrhage, and cervical stenosis (22).

Each technique has advantages and limitations. Therefore, the choice of procedure should be individualized based on institutional resources, lesion size and depth, surgeon expertise, and patient-related factors. Electrocautery conization offers good hemostasis and generally lower complication rates but may cause thermal injury to adjacent tissues and may limit precise excision in small-radius cones (23).

Table (4): Comparison of cold knife, laser, and LEEP procedure **(24)**

	Mean operative time	**Mean blood loss**	**Mean cone volume**	**Difficulty of technique**	**Cost**	**Evaluation of margin**
Cold knife	acceptable	acceptable	superior	acceptable	superior	superior
Laser	acceptable	acceptable	Acceptable	acceptable	inferior	acceptable
LEEP	superior	superior	acceptable	superior	acceptable	inferior

The procedural scheme for laser conization is illustrated in Table 4. Briefly, the patient is placed in the lithotomy position, and a vaginal speculum is inserted. Acetic acid or Schiller's solution is applied to delineate the extent of the surgical resection. Hemostatic sutures using 2-0 Vicryl are placed at the 3 and 9 o'clock positions. Local injection of a vasoconstrictor is not routinely used. Four to eight sutures of 3-0 Vicryl are placed just inside the lesion margin to retract the tissue, and a knot is tied at the 12 o'clock position to facilitate orientation of the excised specimen (24).

The width and depth of conization are determined individually according to colposcopic findings. After marking the incision line 3–5 mm beyond the outer margin using small laser spots, the cervix is excised with a laser beam. If bleeding occurs during the procedure, suction is applied as needed. Once the desired depth is achieved, the upper margin is excised using a scalpel to allow accurate histopathological evaluation of the endocervical surgical margin.

Following specimen removal, hemostasis and vaporization are achieved using a defocused laser beam or ball electrode. Additionally, the outer margins are vaporized to reduce the risk of recurrence in cases with positive surgical margins. An 8 Fr Nelaton catheter is usually inserted into the uterine cavity to prevent cervical stenosis and is typically removed approximately one week after conization; however, catheter insertion may be omitted. An absorbable hemostatic agent, such as oxidized cellulose, is placed on the wound surface (24).

When using loop electrosurgical excision procedures (LEEP/LLETZ), excision in multiple fragments may complicate histopathological assessment. Therefore, surgeons should clearly inform the pathologist about the orientation of the resected specimens. If cold knife conization (CKC) is performed, care should be taken to

minimize complications such as hemorrhage and cervical stenosis (24). Current evidence is insufficient to support the routine use of antibiotics for the prevention of infectious complications following conization; therefore, prophylactic antibiotics are not recommended (25).

The loop electrosurgical excision procedure is relatively simple and rapid, is associated with few complications, and provides an adequate specimen for histopathological examination. However, it may cause thermal damage to adjacent tissues and may be technically challenging when large tissue areas are involved. Lidocaine may be used for local anesthesia and to reduce bleeding. Using a wire loop, cervical tissue is excised in a single movement and sent for histopathological examination (26).

Loop electrosurgical excision procedure (LEEP) is commonly used for the diagnosis and treatment of cervical intraepithelial neoplasia. It allows removal of tissue samples from the cervix and surrounding areas and has distinct advantages and limitations depending on the clinical context (27).

An increased rate of HPV infection has been reported among medical personnel performing electrocautery or diathermic excisional procedures. Smoke-generating procedures pose a potential occupational hazard, as HPV DNA has been detected in the nasal epithelium of exposed healthcare workers. The reported infection rate ranges from 9% to 10% among clinicians treating HPV-positive patients, compared with 2%–3% in the general population. The use of KN95 masks has been associated with a marked reduction in infection risk, with reported rates approaching zero (26).

During colposcopy, a punch biopsy may be performed to confirm or exclude high-grade cervical intraepithelial neoplasia in women with abnormal cervical cytology, including CIN grade II or III. Punch biopsy is performed using specialized forceps such as Kevorkian, Tischler-Morgan, Townsend, Keys, or standard cervical punch biopsy forceps (28). A schematic description of punch biopsy and LEEP techniques is presented in Table 5.

Table (5): Comparison Between Punch Biopsy and Loop Electrosurgical Excision Procedure (LEEP) **(29)**

Parameters	**Punch Biopsy**	**Loop Electrosurgical Excision Procedure (LEEP)**
Characteristic		
Sampling methods	Use the punch biopsy tool to remove a small piece of tissue.	Use the loop electrosurgical excisional tool, which has a heated circular wire to cut and remove a large portion of the affected tissue.
Sampling depth	From the top layer of tissue (epithelium) and a little from the bottom layer.	Deeper layer, including the epithelial layer and some of the stromal layer.
Size of samples	Small sample (3-4 mm in diameter)	Larger and thicker samples
Indication	Used to obtain small samples to diagnose or evaluate pathological conditions such as precancerous lesions or early cancer	LEEP is typically used to take larger samples and for the removal of larger precancerous lesions or early cancers.
Advantage	a.Simple and faster procedures b. Less invasive c. Cost-effective	a. Better sample quality b. Performing the therapeutic benefit to remove larger and potentially malignant lesions c. High accuracy
Disadvantage	a. Limited sample size b. Not suitable for large lesions	a. More invasive b. Higher risk of complications, including

		infection and bleeding

Management of cervical Intraepithelial Neoplasia:

Human papillomavirus (HPV) infection can be prevented through vaccination. HPV vaccination is recommended for individuals aged 11–26 years and, in carefully selected cases, for individuals older than 27 years. Vaccination is also recommended for women with a history of cervical dysplasia and for patients with vulvar warts. Although HPV vaccination has no therapeutic effect on existing lesions, a reduction in recurrence rates has been observed. Recurrence was reported to be 1.9% in vaccinated patients compared with 5.9% in unvaccinated patients with CIN 2 (30).

The choice of treatment depends primarily on the histological diagnosis. However, it is also influenced by cytological findings, patient age, future fertility plans, colposcopic findings, and the presence of endocervical involvement. Additional factors include lesion grade, availability of medical resources, surgeon experience, and patient preference (31).

Low-Grade Lesions (ASC-US and Low-Grade Squamous Intraepithelial Lesions)

Most low-grade lesions regress spontaneously within 24 months. Therefore, surveillance is recommended when colposcopic findings are satisfactory. Follow-up typically consists of cervical cytology every 6 months. Hysterectomy is not an appropriate treatment option for low-grade lesions (32).

Current recommendations for cytologically diagnosed low-grade intraepithelial lesions are based on co-testing results. Approximately 80% of women with low-grade cytological abnormalities have a positive HPV test. However, in cases where cytology indicates a low-grade lesion and HPV testing is negative, co-testing is recommended after one year. If both tests are negative, repeat co-testing is advised after three years.

In women aged 21–24 years with low-grade cytological abnormalities, annual testing for two years is recommended. The incidence of cervical cancer in women younger than 25 years is very low (approximately 1.4 per 100,000 women per year), and HPV-related lesions in this age group frequently regress spontaneously. Colposcopy is indicated if follow-up cytology reveals ASC-H or high-grade squamous intraepithelial lesions (HSIL).

In postmenopausal women, low-grade lesions may be monitored every six months using co-testing or colposcopy. If HPV testing is negative or no dysplasia is identified on colposcopy, repeat co-testing after one year is appropriate. Colposcopy is indicated if ASC-US or high-grade abnormalities are detected (33).

When CIN 1 is confirmed on biopsy following ASC-US or low-grade cytology, co-testing should be performed after one year. If results are negative, the patient may return to routine screening. Persistent CIN 1 for two years may be managed conservatively or treated as a high-grade lesion. If progression to CIN 2 or higher is detected, treatment is required. When CIN 1 is preceded by ASC-H or HSIL, closer follow-up is necessary, including excisional biopsy and careful reassessment (34).

In women aged 21–24 years, a conservative approach is recommended. Cytology should be performed every six months, and colposcopy every two years if high-grade cytology or ASC-H precedes the biopsy. If CIN 2 or worse is suspected, biopsy is required. CIN 1 lesions in this age group should not be treated (35).

High-Grade Squamous Intraepithelial Lesions

High-grade squamous intraepithelial lesions are relatively uncommon, accounting for approximately 0.5–1% depending on population screened of cytological specimens. However, when high-grade lesions are detected cytologically, there is a 70–75% likelihood of identifying CIN 2 or CIN 3 on colposcopy, biopsy, or excision (36).

Due to the high risk of persistence and progression, close surveillance is mandatory regardless of age or menopausal status. In patients with biopsy-confirmed CIN 2 or CIN 3 and satisfactory colposcopy, ablative

methods (e.g., cryotherapy, electrocautery, laser vaporization) or excisional methods (e.g., LEEP, laser conization, cold knife conization, or hysterectomy) are acceptable treatment options (37).

Colposcopy is indicated for cytological diagnoses of ASC-US with positive HPV testing, HSIL, ASC-H, or atypical glandular cells (AGC). If colposcopy is unsatisfactory or endocervical curettage is positive following high-grade cytology, excisional treatment is recommended for both diagnostic and therapeutic purposes (38).

All histologically confirmed CIN 2 or CIN 3 lesions should be managed with excision or ablation of the transformation zone unless the patient is pregnant. The "see-and-treat" approach may be considered in low-resource settings or in patients with poor compliance. In women aged 21–25 years with CIN 2, regression rates are high (28% at 1 year, 63% at 2 years, and 68% at 3 years). Conservative management with colposcopic surveillance every six months may be considered, with excision recommended if the lesion persists beyond two years (39).

In women who have completed childbearing, positive surgical margins following excision necessitate definitive surgical management, such as extrafascial hysterectomy. Recurrence rates may reach 16% in cases with positive margins, compared with approximately 4% in cases with negative margins (40).

Glandular Lesions

For all glandular abnormalities, colposcopy and endocervical curettage are recommended regardless of HPV test results. Endometrial sampling is advised in women older than 35 years with AGC or adenocarcinoma in situ (AIS).

If CIN 2 or higher is excluded, surveillance every 12–24 months is appropriate. If follow-up results remain negative, surveillance should continue for three years. Conservative management may be considered in women desiring future fertility. Excisional procedures are recommended when CIN or AIS is detected in endocervical samples. Re-evaluation after six months using co-testing, colposcopy, and endocervical sampling is advised (41).

Treatment Options

Treatment modalities are broadly classified into excisional procedures (e.g., LEEP, laser conization, cold knife conization) and ablative procedures (e.g., cryotherapy, laser ablation). Treatment selection should be individualized based on lesion characteristics, patient factors, and clinician expertise.

Ablative therapy requires satisfactory colposcopy, absence of invasive disease, benign endocervical curettage, and complete visualization of the lesion. Advantages include lower cost and reduced risk of preterm delivery. However, no tissue specimen is available for histopathological evaluation. Laser ablation is particularly useful for high-grade lesions but is limited by high cost (42).

Excisional procedures remove a cone-shaped portion of the cervix and serve both diagnostic and therapeutic purposes. Surgical expertise is essential to minimize complications. Cold knife conization requires anesthesia and hospitalization and is associated with higher morbidity. CO_2 laser conization can be performed on an outpatient basis, preserves fertility, and allows excellent healing but is costly and requires advanced training (43,44).

Loop diathermy conization is a monopolar electrosurgical technique that is quick, economical, and effective. However, incomplete excision may occur in 10-30% of cases, and negative cone rates range from 14% to 30%, potentially leading to overtreatment or compromised fertility if excessive cervical tissue is removed (32).

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