

Algorithms for management of Cervical cancer

FIGO staging system, 2009

Stage I

The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded)

Stage IA: Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion ≤ 5 mm and largest extension ≤ 7 mm

Stage IA1: Measured stromal invasion of ≤ 3.0 mm in depth and extension of ≤ 7.0 mm.

Stage IA2: Measured stromal invasion of >3.0 mm and ≤ 5.0 mm with an extension of not >7.0 mm

Stage IB: Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA*

Stage IB1: Clinically visible lesion ≤ 4.0 cm in greatest dimension

Stage IB2: Clinically visible lesion >4.0 cm in greatest dimension

Stage II

Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina

Stage IIA: Without parametrial invasion

Stage IIA1: Clinically visible lesion ≤ 4.0 cm in greatest dimension

Stage IIA2: Clinically visible lesion >4 cm in greatest dimension

Stage IIB: With obvious parametrial invasion

Stage III

The tumor extends to the pelvic wall and/or involves lower third of the vagina and or causes hydronephrosis or non-functioning kidney**

Stage IIIA: Tumor involves lower third of the vagina, with no extension to the pelvic wall

Stage IIIB: Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney

Stage IV

The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum.

A bullous edema, as such, does not permit a case to be allotted to Stage IV

Stage IVA: Spread of the growth to adjacent organs.

Stage IVB: Spread to distant organs.

*All macroscopically visible lesions—even with superficial invasion—are allotted to stage IB carcinomas. Invasion is limited to a measured stromal invasion with a maximal depth of 5.00 mm and a horizontal extension of not >7.00 mm. Depth of invasion should not be >5.00 mm taken from the base of the epithelium of the original tissue—superficial or glandular. The depth of invasion should always be reported in mm, even in those cases with “early (minimal) stromal invasion” (~ 1 mm). The involvement of vascular/lymphatic spaces should not change the stage allotment.

** On rectal examination, there is no cancer-free space between the tumor and the pelvic wall. All cases with hydronephrosis or non-functioning kidney are included, unless they are known to be due to another cause.

Cervical cancer FIGO Stage I a Microinvasive carcinoma (invasion ≤ 5 mm)

Recommended work-up

- Vaginal and rectal examination, exfoliative cytology (Papanicolaou smear), colposcopy, biopsy and/or endocervical curettage (ECC), conization or Loop electrosurgical procedure (LEEP)
- Histopathological finding with all standard tumor parameters
- Laboratory analyses: WBC, biochemical analyses
- Imaging: Chest X-ray, pelvic and abdominal ultrasound

Diagnosis is based on conization!

Conization

Necessary HP parameters:²

- Depth of invasion
- Width of the tumor
- Tumor differentiation
- Lympho-vascular space invasion (LVSI)
- Resection margins

Margins clear
ECC negative

Stage Ia1
LVSI negative

Conization if preservation of fertility is desired

or

Simple (extrafascial, type A⁶) hysterectomy with or without salpingoophorectomy

Margins and/or
ECC positive for dysplasia

• Stage Ia1 with extensive LVSI
• Stage Ia2

Conization or radical trachelectomy if preservation of fertility is desired

or

Modified radical hysterectomy (type B⁶)

and

Pelvic lymphadenectomy

- Repeated conization
- Modified radical hysterectomy (type B⁶) if re-conisation is not possible
- ± pelvic lymphadenectomy

Recommended follow-up

Every 3 months after completed therapy during the first year; every 6 months up to 5 years. Annually afterwards. Investigations in addition to gynaecological examination, including cytology and colposcopy, should be performed depending on symptoms, local findings and general condition of the patient

Cervical cancer FIGO Stage Ib - IIa Squamocellular, Adenocarcinoma, Adenosquamous

Recommended work-up

Necessary investigations:

- Vaginal and rectal examination, colposcopy, biopsy and/or endocervical curettage (ECC); conization or loop electrosurgical procedure (LEEP) if needed for definitive diagnosis
- Histopathological finding with all standard tumor parameters
- Laboratory analyses: WBC, biochemical analyses including check for renal function and Hb
- Imaging: Chest X-ray, abdominal and pelvic ultrasound (size and position of the tumor and tumor volume/cervix ratio)

Optional investigations:

Pelvic NMR, CT of the abdomen (PET/CT if possible), cystoscopy, rectoscopy, IVU or sonographic renal examination. Involvement of the bladder or rectum should be confirmed histologically

Radical surgery

or

Chemo-radiation

Neoadjuvant chemotherapy followed by radiation or surgery is an option for locally advanced tumors (Ib2 and IIa2) but awaits confirmatory evidence from controlled clinical trials.

- Uterus with paracervical tissues and upper part of vagina (radical, type C⁴ hysterectomy) + pelvic lymphadenectomy
- or
- Entire cervix with paracervical tissues (radical trachelectomy) if fertility is desired + pelvic lymphadenectomy
- or
- Upper part of vaginal cuff, paracervical tissues + pelvic lymphnodes in case of previous simple hysterectomy

- * At least 2 cm distance from the resection margins is desirable
- ** In premenopausal women ovaries can be retained; if so tranposition is advised.
- *** For the decision of further management, all necessary histopathologic parameters⁴ should be requested

- Medical contra-indications for surgery
- Ib2/IIa2 tumors in selected cases
- Anterior vaginal extension
- Invasive cancer after simple hysterectomy
- Choice of the patient

Negative nodes

GOG score*

* consider using GOG score as a guide for adjuvant treatment⁵

Low risk
(GOG score < 120)

High risk
(GOG score > 120)

Follow up

Radiation
± Chemotherapy

Radiation
± Chemotherapy

Concomitant
Chemo-radiation

- Positive nodes (1-3)
- Poorly differentiated or undifferentiated tumor (G3)
- LVSI present
- Primary tumor (tumor-cervix volume) > 3 cm
- Endocervical invasion (barrel shaped cervix)
- Inadequate surgery
- Insufficient HP (if report of all necessary parts is missing)

- Positive resection margins
- Involvement of parametria
- Residual tumor
- Multiple positive nodes (>3)

Recommended follow-up

Every 3 months after completed therapy during the first year; every 6 months up to 5 years. Annually afterwards. Investigations in addition to gynaecological examination should be performed depending on symptoms, local findings and general condition of the patient

Cervical cancer FIGO stage IIb- IV

Recommended work-up

- Vaginal and rectal examination, biopsy or endocervical curettage (ECC)
- Histopathological finding with all standard tumor parameters
- Laboratory analyses: WBC, biochemical analyses including check for renal function and Hb
- Imaging: Chest X-ray, abdominal and pelvic ultrasound
- Pelvic NMR, CT of the abdomen (PET/CT if possible), cystoscopy, rectoscopy, IVU or sonographic renal examination. Involvement of the bladder or rectum should be confirmed histologically

Pelvic MRI and Abdominal CT

Para-aortic nodes (PALN) negative
(=not enlarged)

Pelvic (± para-aortic) radiation
+ brachytherapy
+ concomitant chemotherapy

Pelvic or para-aortic nodes (PALN) positive
(enlarged ≥ 2 cm)
Adnexal mass

CT of the lungs & mediastinum

CT negative

Pelvic radiation (with para-aortic if PALN are positive) +
brachytherapy + concomitant chemotherapy

* Consider:

- resection of adnexal mass and/or extraperitoneal resection of enlarged nodes
- Sequential chemo and Concomitant ChemoRadioTherapy /External Beam RadioTherapy (CCRT/EBRT)

CT positive

Palliative pelvic RT
± Palliative chemotherapy

*Stage IVa

- with vesicovaginal fistula: if pelvic, abdominal and chest imaging exclude distant metastases primary pelvic exenteration can be considered
- NACT may be offered to large bulky tumors to downsize tumor prior to CCRT



Recommended follow-up

Every 3 months after completed therapy; every 6 months up to 5 years. Annually afterwards. Investigations in addition to gynaecological examination should be performed depending on symptoms, local findings and general condition of the patient

Cervical cancer - recurrence -

Recommended work-up

- Vaginal and rectal examination, biopsy - histopathological confirmation of recurrence
- Laboratory analyses: WBC, biochemical analyses including check for renal function and Hb
- Imaging: Chest X-ray, pelvic and abdominal ultrasound, pelvic NMR and CT of the lungs and abdomen; (PET/CT if possible)
- Cystoscopy, rectoscopy, IVU or sonographic renal examination

Lungs & abdominal CT

Pelvic recurrence

No previous radiation

- Options include:
- Chemo-radiation
 - Neoadjuvant chemotherapy (NACT)
 - Supportive care

Previous radiation

Central pelvic recurrence

- Options include
- Radical hysterectomy in tumor <2 cm
 - Pelvic exenteration
 - Neoadjuvant chemotherapy (NACT) + surgery
- Other options if surgery is not possible:
- Re-irradiation
 - Neoadjuvant chemotherapy (NACT) + radiation
 - Systemic therapy
 - Supportive care

Sidewall pelvic recurrence

- Options include:
- Resection of isolated disease
 - Systemic therapy
 - Supportive care

Extrapelvic recurrence

- Options include:
- Palliative radiotherapy or chemo-radiation
 - Systemic therapy
 - Supportive care
- * Resection in selected cases (in particular paraaortic nodes) may be considered



Recommended follow-up

Every 3 months for two years or more often if clinically indicated. Every 4-6 months thereafter. Annually afterwards. Investigations in addition to gynaecological examination should be performed depending on symptoms, local findings and general condition of the patient

Cervical cancer additional explanations

1. FIGO staging of invasive cervical cancer

Source: FIGO COMMITTEE ON GYNECOLOGIC ONCOLOGY. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. International Journal of Gynecology and Obstetrics, 2009; 105: 103-104

2. Necessary histopathologic (HP) parameters for microinvasive cancer

- Depth of invasion
- Width of the tumor
- Tumor differentiation
- Lympho-vascular space invasion (LVSI)
- Resection margins

3. Necessary histopathologic (HP) parameters for invasive cervical cancer

- Dimensions of the tumor
- Stromal invasion / depth of the wall involved
- Tumor differentiation
- Lympho-vascular space invasion (LVSI)
- Length and status of parametria
- Length of vaginal cuff
- Status of resection margins (vagina, parametria)
- Minimal distance between the tumor and resection margin
- Number and status of lymph nodes

*all necessary parts should be requested if possible

4. Prognostic factors for invasive Cervical cancer

For adjuvant radiation

- High risk node negative patients
- Positive nodes (1-3)
- Poorly differentiated or undifferentiated tumor (G3)
- Lympho-vascular space invasion (LVSI)
- Primary tumor (tumor-cervix volume) >3 cm
- Endocervical invasion (barrel shaped cervix)
- Inadequate surgery
- Insufficient HP report (i.e. report of all necessary parts is missing)

For adjuvant chemo-radiation

- Positive resection margins
- Involvement of parametria
- Residual tumor
- Multiple positive lymph nodes (>3)

5. GOG scoring system

Delgado G, Bundy B, Zaino R et al. Prospective surgical-pathological study of disease free-interval in patients with stage Ib squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Gynecol Oncol, 1990; 38:352-379

6. Classification of radical hysterectomy

Querleu D, Morrow CP, Classification of radical hysterectomy. Lancet Oncol 2008; 9:297-303 & Gynecol Oncol 2009; 115:314-315

Cervical cancer

Squamocellular, Adenocarcinoma, Adenosquamous

Recommended work-up

Necessary investigations:

- Vaginal and rectal examination, colposcopy, biopsy and/or endocervical curettage (ECC); conization or loop electrosurgical procedure (LEEP) if needed for definitive diagnosis
- Histopathological finding with all standard tumor parameters
- Laboratory analyses: WBC, biochemical analyses including check for renal function and Hb
- Imaging: Chest X-ray, abdominal and pelvic ultrasound (size and position of the tumor and tumor volume/cervix ratio)

Optional investigations:

- Pelvic NMR, CT of the abdomen (PET/CT if possible), cystoscopy, rectoscopy, IVU or sonographic renal examination. Involvement of the bladder or rectum should be confirmed histologically

*Stage of the disease is determined using FIGO classification¹

FIGO Ia

- Diagnosis is based on conization; resection margins should be clear
- Further decision depends on the presence of poor histologic prognostic factors²

FIGO Ia1
LVSI negative

FIGO Ia1, LVSI positive
FIGO Ia2

- Conization
- or
- Simple hysterectomy (type A⁶)

- Conization/radical trachelectomy
- or
- Modified radical hysterectomy (type B⁶)
- and
- Pelvic lymphadenectomy

Follow-up

FIGO Ib-IIa

Surgery

or

Chemo-radiation

- Medical contra-indications for surgery
- Ib2/IIa tumors
- Anterior vaginal extension
- Invasive cancer after simple hysterectomy
- Choice of the patient

- Radical hysterectomy (type C⁶)
- or
- Radical trachelectomy
- or
- Resection of the upper part of vagina and parametrectomy in case of previous simple hysterectomy
- and
- Pelvic lymphadenectomy
- * Decision about further therapy is based on the presence of adverse histological factors

No adverse prognostic factors

Follow-up

Adverse prognostic factors⁴ present

Adjuvant therapy
(Radiation ± Chemotherapy)

FIGO IIb-IV

Concomitant chemoradiation
or
Radical radiation only if unfit for chemotherapy

* Stage IV1 with vesicovaginal fistula: if pelvic, abdominal and chest CT exclude distant metastases, primary pelvic exenteration can be considered

Neoadjuvant chemotherapy followed by radiation or surgery is an option for locally advanced tumors, but awaits confirmatory evidence from controlled clinical trials.



Recommended follow-up

Every 3 months after completed therapy during the first year; every 6 months up to 5 years Annually afterwards. Investigations in addition to gynaecological examination should be performed depending on symptoms, local findings and general condition of the patient