

Research Article

Development of a management guide wheel for cervical cancer

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Keywords: Cervical cancer; Surgical staging; Radiotherapy; Chemotherapy; Systemic therapy; FIGO classification; Guidelines; Persistent or recurrent disease; Therapy for relapse; Surveillance; Surgical node status; Trachelectomy; Radical hysterectomy; Distant metastases

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Abstract

We designed and developed a management guide wheel for cervical cancer to facilitate a standard approach and improve the quality of care in managing patients diagnosed with different stages of cervical cancer. Each step of the wheel considers the patient's current medical condition, FIGO stage, and the possible treatment modalities for cervical cancer in her case. We reviewed existing international guidelines on the management of cervical cancer and compared their respective recommendations. This guide wheel is based on recommendations by the following organizations: the National Comprehensive Cancer Network (NCCN), the Society of Gynecologic Oncology (SGO), the European Society of Gynaecological Oncology (ESGO), the European Society for Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO), the British Gynaecological Cancer Society (BGCS) and the International Federation of Gynecology and Obstetrics (FIGO).

Abbreviations

ASCO: American Society of Clinical Oncology; BGCS: British Gynaecological Cancer Society; CC: cervical cancer; CT: Computed Tomography; EBRT: External Beam Radiotherapy; ESGO: European Society of Gynaecological Oncology; ESMO: European Society for Medical Oncology; FIGO: International Federation of Gynecology and Obstetrics; IORT: Intra-Operative Radiotherapy; LN: Lymph Node; LND: Lymph Node Dissection; LVSI: Lymphovascular Space Invasion; MRI: Magnetic Resonance Imaging; NCCN: National Comprehensive Cancer Network; PET: Positron Emission Tomography; RH: Radical Hysterectomy; SGO: Society of Gynecologic Oncology; TNM: Tumors, Nodes, and Metastases.

Introduction

Cervical Cancer (CC) is the fourth most common cancer in women worldwide and the second most common cancer in developing countries [1-7]. The mainstay of treating CC involves surgery, radiotherapy, chemotherapy, or a combination of those [6-9]. Early-stage CC is usually asymptomatic and patients present with symptoms in advanced stages [4,5,10]. CC can be preventable with effective screening and vaccination programs [4,5,11,12]. Early detection of pre-malignant states before they develop into cancer leads to earlier treatment and hence, a better outcome [12]. In fact, early-stage CC has a cure rate of 80-95% [8]. 30% of CC in developed countries are Stage IB or higher compared to 60% in developing countries due to

the unavailability of well-established screening programs in the latter [2,12].

Various health organizations globally have developed sets of guidelines on the management of CC. We compared recommendations by the National Comprehensive Cancer Network (NCCN), the Society of Gynecology (SGO), the European Society of Gynaecological Oncology (ESGO), the European Society for Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO), the British Gynaecological Cancer Society (BGCS) and the International Federation of Gynecology and Obstetrics (FIGO) [4-6,9,10,13,14]. The NCCN guidelines for managing cancer cervix is one of the most frequently updated and comprehensive guidelines available [4].

We developed a management guide wheel for CC based on the recommendations of the compared guidelines but mainly reflecting the most recently updated guidelines by NCCN. This guide wheel aims to serve healthcare professionals in finding a quick and comprehensive display of the recommended steps and alternatives to manage patients diagnosed with CC when counseling patients. We are also comparing the guidelines covered here in another research article to highlight the similarities and differences in their respective recommendations. We developed a similar guide wheel for the management of uterine neoplasms [15]. We also developed a guide wheel describing the management of abnormal pap

smear results and a comparison of the recommendations of international organizations [12,16].

About this guide wheel

This guide wheel includes recommendations and algorithms for managing patients with CC as per the guidelines compared during this study (Figure 1). It consists of a base (Figure 2) and an inner wheel (Figure 3). There is more information on how to use the guide wheel on the back of the base (Figure 4).

There are thirteen possible modalities of treatment with the different options under those modalities mentioned on the inner wheel as follows:

- Primary Therapy: a. Surgery; b. Radiotherapy; c. Chemotherapy; d. Imaging; e. Lymph node (LN) status
- Surgical Therapy: a. Conization; b. Re-Conization; c. Hysterectomy (A. Simple; B. Modified Radical Hysterectomy (RH); C. RH); d. Lymphadenectomy (Pelvic; Para-aortic); e. Trachelectomy; f. Completion; g. Resection
- Additional Workup: a. Imaging; b. Biopsy; c. Pathology; d. Surgical Staging; e. Exploration

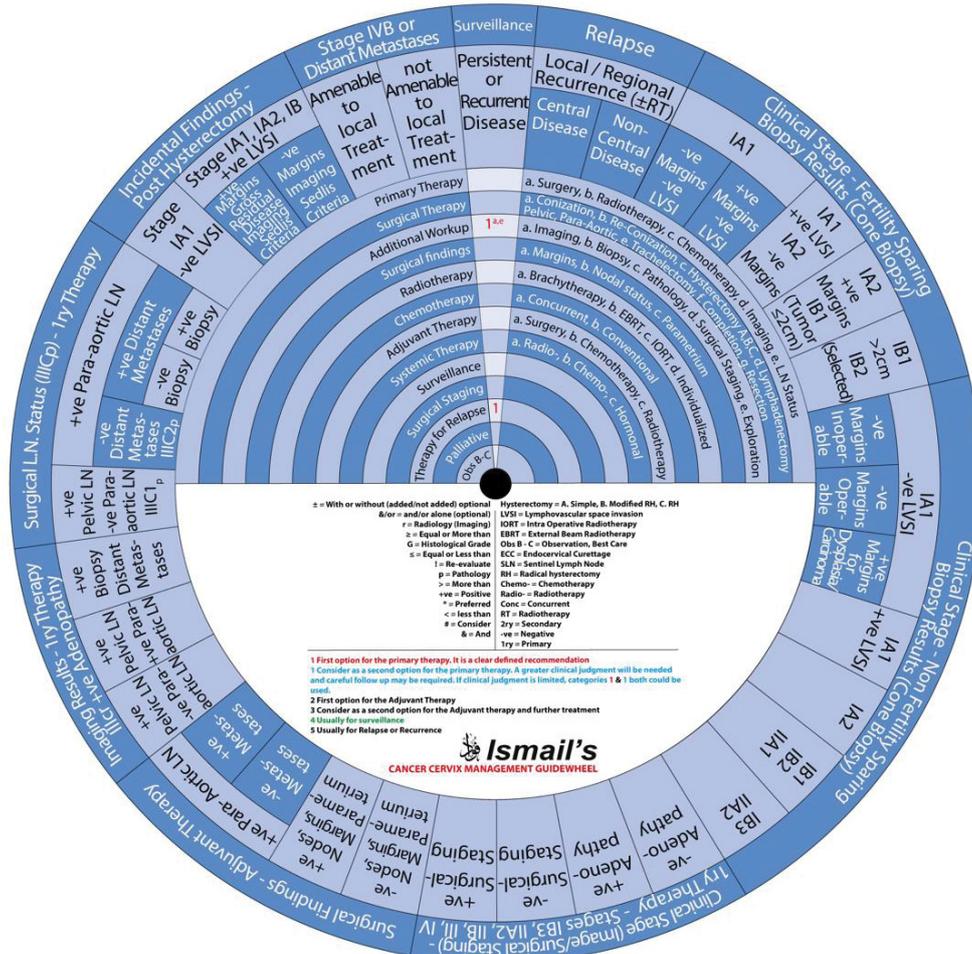


Figure 1: The guide wheel fully assembled demonstrates the surveillance pathway when managing persistent or recurrent cervical cancer.

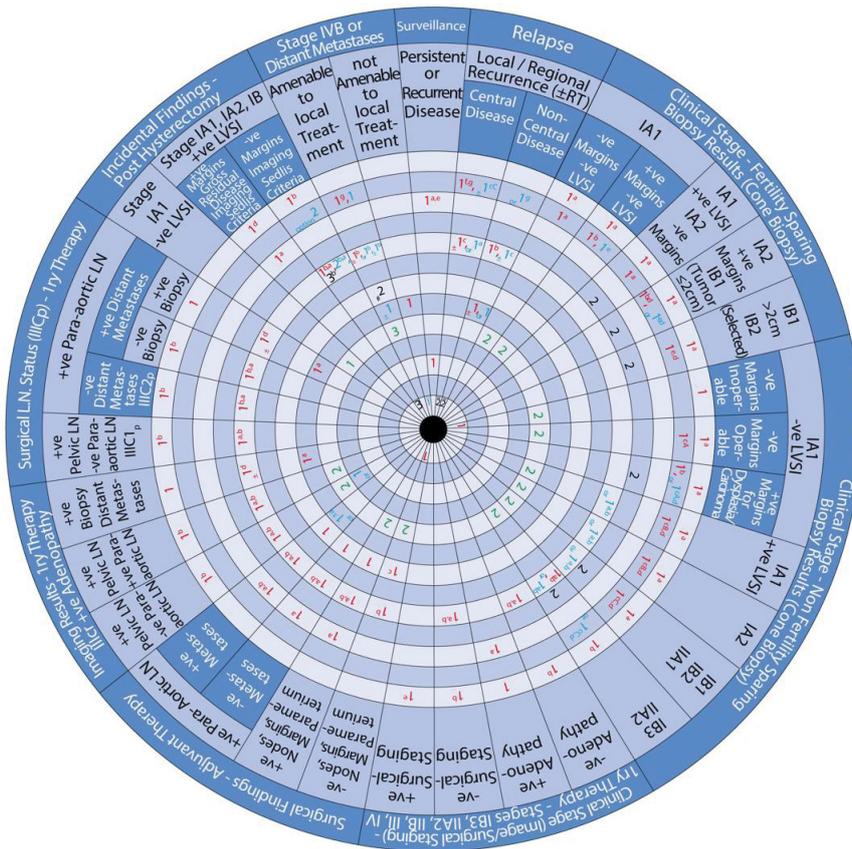


Figure 2: The base of the guide wheel demonstrates the stages of cervical cancer and the color-coded treatment modalities.

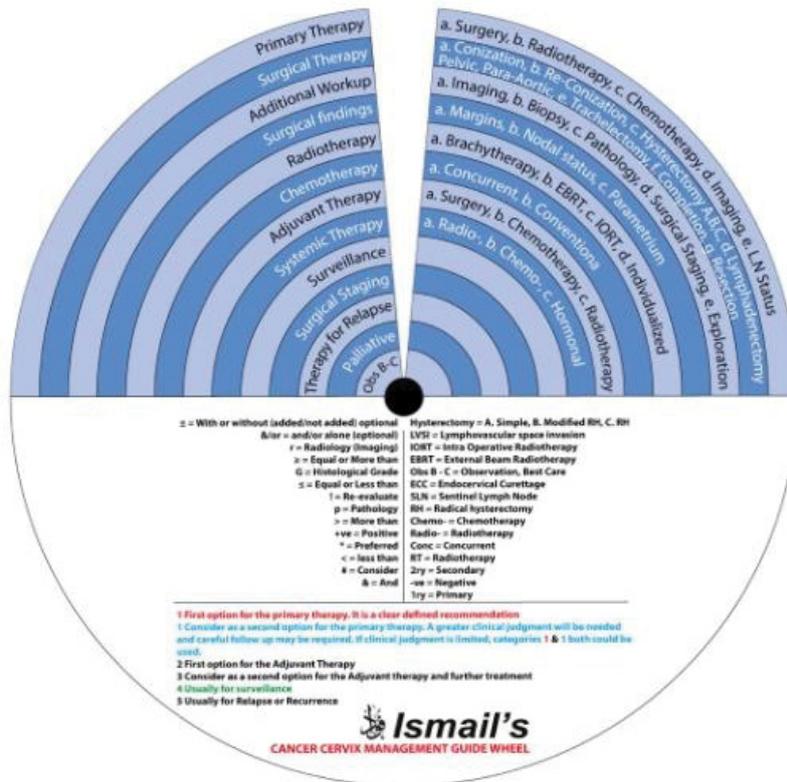


Figure 3: The inner wheel of the guide wheel that is placed on top of the base demonstrates the various treatment modalities and the available options for each.

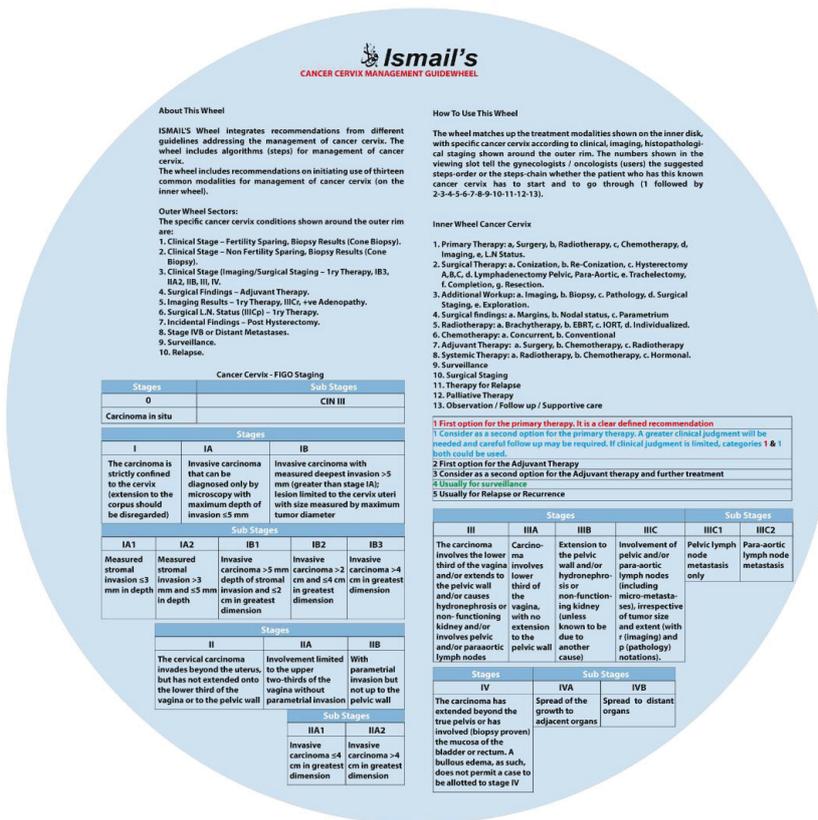


Figure 4: The back of the guide wheel describes how to use the wheel in addition to the FIGO staging system of cervical cancer.

- Surgical findings: a. Margins; b. Nodal status; c. Parametrium
- Radiotherapy: a. Brachytherapy; b. External Beam Radiotherapy (EBRT); c. Intraoperative Radiotherapy (IORT); d. Individualized
- Chemotherapy: a. Concurrent; b. Conventional
- Adjuvant Therapy: a. Surgery; b. Chemotherapy; c. Radiotherapy
- Systemic Therapy: a. Radiotherapy; b. Chemotherapy; c. Hormonal
- Surveillance
- Surgical Staging
- Therapy for Relapse
- Palliative Therapy
- Observation, Follow-up and Supportive care.

How to use this guide wheel

The guide wheel aligns the treatment modalities on the inner wheel with the particular stage of cervical cancer diagnosed, on the outer wheel, following clinical, radiological, and histopathological investigations. The viewing slot displays the steps recommended to follow in chronological order to manage the patient under consideration (Figure 1).

The base of the guide wheel displays color-coded treatment modalities in order. The numbers signify the steps and alternative options as follows:

- 1 → This marks the first option for Primary Therapy. It is a clearly defined recommendation.
- 1 → This is a second option for Primary Therapy. It might require greater clinical judgment and careful follow-up. If the clinical judgment is limited, either option 1 or 1 could be used.
- 2 → This marks the first option for Adjuvant Therapy.
- 3 → This is considered as a second option for Adjuvant Therapy and further treatment.
- 4 → This is usually reserved for surveillance.
- 5 → This is usually reserved for Relapse or Recurrence.

Abbreviations used on the wheel include the following:

| | | | |
|---|---|------|-------------------------------|
| ± | There is an option to add or to not add (with or without) | ! | Re-evaluate |
| > | More than | LVSI | Lymphovascular space invasion |
| < | Less than | ECC | Endocervical Curettage |
| ≥ | Equal or more than | RH | Radical hysterectomy |
| ≤ | Equal or less than | RT | Radiotherapy |
| # | Consider | SLN | Sentinel Lymph Node |



| | | | |
|------|-------------------------|----------|------------------------------|
| * | Preferred | EBRT | External Beam Radiotherapy |
| & | And | IORT | Intra Operative Radiotherapy |
| &/or | And/or alone (optional) | 1ry | Primary |
| r | Radiology (Imaging) | 2ry | Secondary |
| p | Pathology | Conc | Concurrent |
| G | Histological Grade | Radio- | Radiotherapy |
| +ve | Positive | Chemo- | Chemotherapy |
| -ve | Negative | Obs, B-C | Observation, Best Care |

The stages of cervical cancer shown on the outer wheel are as follows:

1. Fertility-Sparing Options for Stages IA1, IA2, IB1, and select IB2 Based on Cone Biopsy Results
2. Non-Fertility Sparing Options for Stages IA1, IA2, IB1, IB2, IB3, IIA1, and IIA2 Based on Cone Biopsy Results
3. Primary Therapy for Stages IB3, IIA2, IIB, III, and IV Based on Imaging or Surgical Staging
4. Adjuvant Therapy Based on Surgical Findings
5. Primary Therapy Based on Imaging Results Demonstrating Positive Adenopathy
6. Primary Therapy Based on Surgical Lymph Node Status
7. Incidental Surgical Finding of Cervical Cancer Post-Hysterectomy
8. Stage IVB or Distant Metastases
9. Surveillance of Persistent or Recurrent Disease
10. Therapy for Relapse

The back of the wheel displays the FIGO staging system for cervical cancer, most recently updated in 2018, as followed by the international guidelines. The table below exhibits the stages of cervical cancer and their definitions [1, 4, 6, 7, 9, 10].

| FIGO Stages and Sub-Classifications | |
|--|--|
| Stage I: The carcinoma is strictly confined to the cervix uteri (extension to the corpus should be disregarded) | |
| IA: Invasive carcinoma that can be diagnosed only by microscopy with a maximum depth of invasion ≤ 5 mm ³ | IA1: Measured stromal invasion < 3 mm in depth IA2: Measured stromal invasion ≥ 3 mm and < 5 mm in depth |
| IB: Invasive carcinoma with measured deepest invasion ≥ 5 mm (greater than stage IA); lesion limited to the cervix uteri | IB1: Invasive carcinoma ≥ 5 mm depth of stromal invasion and < 2 cm in greatest dimension IB2: Invasive carcinoma ≥ 2 cm and < 4 cm in greatest dimension IB3: Invasive carcinoma ≥ 4 cm in greatest dimension |
| Stage II: The cervical carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall | |
| IIA: Involvement limited to the upper two-thirds of the vagina without parametrial involvement | IIA1: Invasive carcinoma < 4 cm in greatest dimension IIA2: Invasive carcinoma ≥ 4 cm in greatest dimension |
| IIB: With parametrial invasion but not up to the pelvic wall | |

Stage III: The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or para-aortic lymph nodes

| | |
|---|---|
| IIIA: Carcinoma involves the lower third of the vagina, with no extension to the pelvic wall | IIIB: Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause) |
| IIIC: Involvement of pelvic and/or para-aortic lymph nodes, irrespective of tumor size and extent (with imaging and pathology notations) | IIIC1: Pelvic lymph node metastasis only IIIC2: Para-aortic lymph node metastasis |

Stage IV: The carcinoma has extended beyond the true pelvis or has involved (biopsy-proven) the mucosa of the bladder or rectum. Bullous edema, as such, does not permit a case to be allotted to stage IV

| | |
|---|--------------------------------------|
| IVA: Spread of the growth to adjacent organs | IVB: Spread to distant organs |
|---|--------------------------------------|

Recommendations on managing patients with cervical cancer using the guide wheel

Sector 1: Fertility-Sparing Options for Stages IA1, IA2, IB1, and select IB2 Based on Cone Biopsy Results (Figure 5)

For patients with stage IA1 cervical cancer with negative margins and negative LVSI:

- 1a: Primary treatment is surgery (1a).
- 1a: Surgical treatment (1) with conization (a).
- 2: The second step is surveillance.

For patients with stage IA1 cervical cancer with positive margins and negative LVSI:

- 1a: Primary treatment is surgery (1a).
- 1b: Surgical treatment (1) with re-conization (b).
- 1e: An alternative is a surgical treatment (1) with trachelectomy (e).
- 2: The second step is surveillance.

For patients with stage IA1 cervical cancer with positive LVSI and stage IA2 with negative margins:

- 1a: Primary treatment is surgery (1a).
- 1e, d: Surgical treatment (1) with conization (e) with pelvic lymphadenectomy with or without para-aortic lymphadenectomy (d). Sentinel LN mapping can be considered.
- or 1a, d: An alternative is a surgical treatment (1) with conization (a) with pelvic lymphadenectomy. Sentinel LN mapping can also be considered if negative margins.
- 2: The second step depends on surgical findings.

For patients with stage IA2 cervical cancer with positive margins and stage IB1 with tumor measuring ≤ 2 cm:

- 1a: Primary treatment is surgery (1a).
- 1e, d: Surgical treatment (1) with conization (e) with

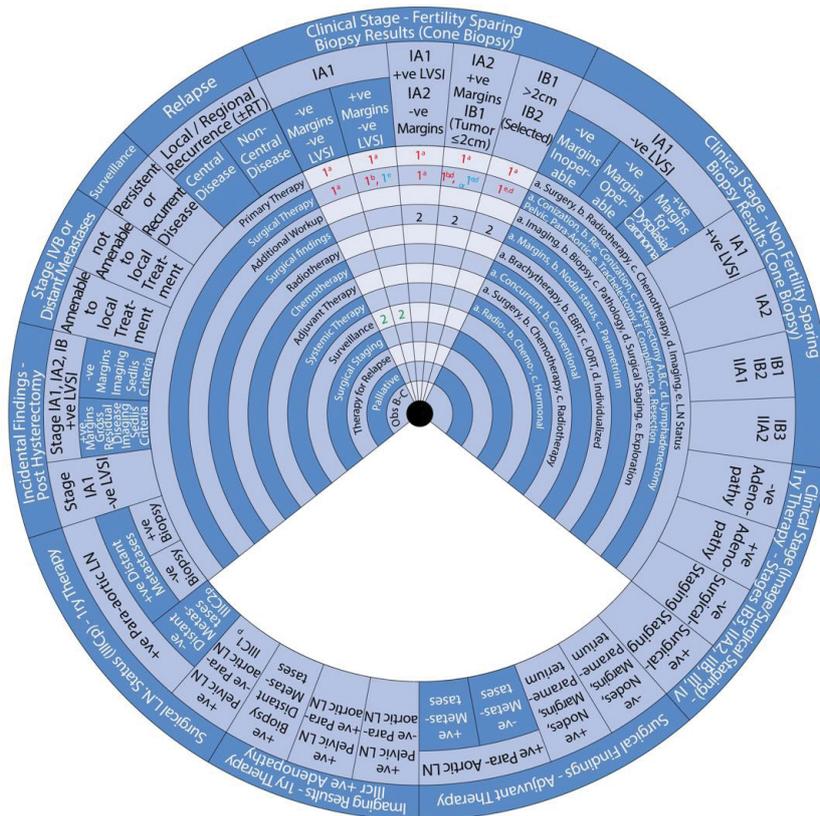


Figure 5: Fertility-Sparing Options for Stages IA1, IA2, IB1, and select IB2 Based on Cone Biopsy Results.

pelvic lymphadenectomy with or without para-aortic lymphadenectomy (d). Sentinel LN mapping can be considered.

- or 1b, d: An alternative is surgical treatment (1) with re-conization (b) with pelvic lymphadenectomy. Sentinel LN mapping can also be considered.
- 2: The second step depends on surgical findings.

For patients with stage IB1 with a tumor measuring > 2 cm and select cases of stage IB2 ≤ 2 cm:

- 1a: Primary treatment is surgery (1a).
- 1e, d: Surgical treatment (1) with radical trachelectomy (e) with pelvic lymphadenectomy with or without para-aortic lymphadenectomy (d). Sentinel LN mapping can be considered.
- 2: The second step depends on surgical findings. This does not apply to patients with small neuroendocrine or gastric type adenocarcinoma of adenoma malignum.

Sector 2: Non-Fertility Sparing Options for Stages IA1, IA2, IB1, IB2, IB3, IIA1 and IIA2 Based on Cone Biopsy Results (Figure 6)

For patients with an inoperable stage IA1 cervical cancer with negative margins and negative LVSI:

- 1: The first step is observation (1).

- 2: The second step is surveillance.
- For patients with an operable stage IA1 cervical cancer with negative margins and negative LVSI:

- 1a: Primary treatment is surgery (1a).
- 1cA: Surgical treatment (1) with simple hysterectomy (cA).
- 2: The second step is surveillance.

For patients with stage IA1 cervical cancer with margins positive for dysplasia or carcinoma but negative LVSI:

- 1a: Primary treatment is surgery (1a).
- 1b: Surgical treatment (1) with re-conization (b) with pathological re-evaluation.
- or 1cA, d: An alternative is surgical treatment (1) with simple hysterectomy (cA) or modified RH with pelvic lymphadenectomy (d). Sentinel LN mapping can also be considered.
- 2: The second step depends on surgical findings.

For patients with stage IA1 cervical cancer with positive LVSI and Stage IA2:

- 1a: Primary treatment is surgery (1a).
- 1cB, d: Surgical treatment (1) with modified RH (cB)

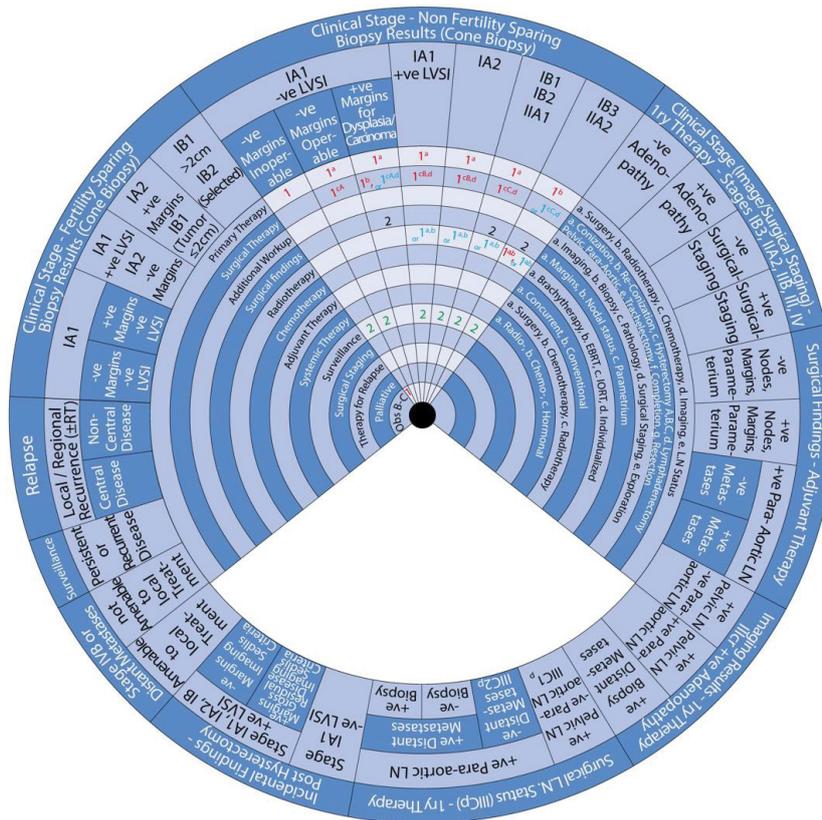


Figure 6: Non-Fertility Sparing Options for Stages IA1, IA2, IB1, IB2, IB3, IIA1 and IIA2 Based on Cone Biopsy Results.

with pelvic lymphadenectomy (d). Sentinel LN mapping can also be considered.

- or 1a, b: An alternative is a radiotherapy (1) with EBRT (b) and brachytherapy (a).
- 2: The second step is surveillance.

For patients with cervical cancer stages IB1, IB2, and IIA1:

- 1a: Primary treatment is surgery (1a).
- 1cC, d: Surgical treatment (1) with RH (cB) and pelvic lymphadenectomy (d) with or without para-aortic lymphadenectomy. Sentinel LN mapping can also be considered.
- or 1a, b: An alternative is a radiotherapy (1) with EBRT (b) and brachytherapy (a) with or without concurrent chemotherapy.
- 2: The second step depends on surgical findings.
- 2: The next step is surveillance.

For patients with cervical cancer stages IB3 and IIA2:

- 1b: Primary treatment is radiotherapy (1b).
- 1a, b: Radiotherapy (1) with EBRT (b) and brachytherapy (a) with concurrent chemotherapy.
- or 1cC, d: An alternative is a surgical treatment (1)

with RH (cC) and pelvic lymphadenectomy (d) with or without para-aortic lymphadenectomy.

- or 1a, b: An alternative is a radiotherapy (1) with EBRT (b) and brachytherapy (a) with or without concurrent chemotherapy and adjuvant hysterectomy.
- 2: The second step depends on surgical findings.
- 2: The next step is surveillance.

Sector 3: Primary Therapy for Stages IB3, IIA2, IIB, III, and IV Based on Imaging or Surgical Staging (Figure 7)

For patients with cervical cancer stages IB3, IIA2, IIB, III, and IV and negative adenopathy:

- 1b: Primary treatment is radiotherapy (1b).
- 1a, b: Radiotherapy (1) with EBRT (b) and brachytherapy (a) with concurrent chemotherapy.

For patients with cervical cancer stages IB3, IIA2, IIB, III, and IV and positive adenopathy:

- 1a: Primary treatment is additional workup with imaging (1a). Further steps depend on the results.

For patients with cervical cancer stages IB3, IIA2, IIB, III, and IV and negative surgical staging:

- 1b: Primary treatment is radiotherapy (1b).

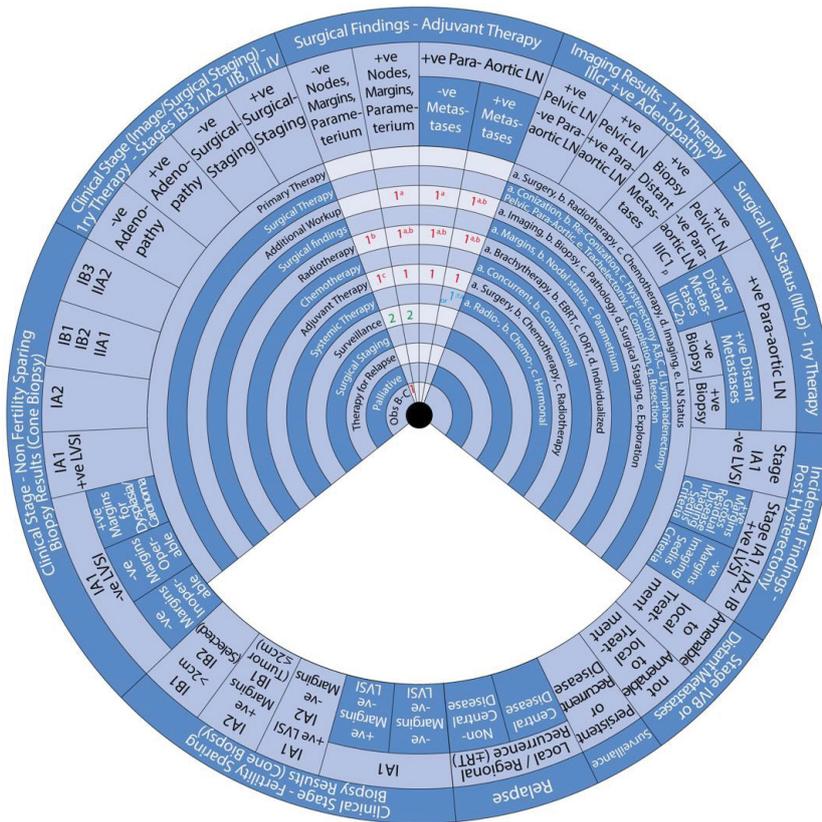


Figure 8: Adjuvant Therapy Based on Surgical Findings.

Sector 5: Primary Therapy Based on Imaging Results Demonstrating Positive Adenopathy (Figure 9)

For patients with cervical cancer and positive pelvic LN but negative para-aortic LN based on imaging:

- 1b: Primary treatment is radiotherapy (1b).
- 1a, b: Radiotherapy (1) with pelvic EBRT (b) and brachytherapy (a) with concurrent chemotherapy with or without para-aortic LN EBRT.
- or 1: An alternative is surgical staging (1) of para-aortic LN.
- 2: The second step is surveillance.

For patients with cervical cancer and positive pelvic LN and para-aortic LN based on imaging:

- 1b: Primary treatment is radiotherapy (1b).
- 1a, b: Radiotherapy (1) with extended-field EBRT (b) and brachytherapy (a) with concurrent chemotherapy.
- 2: The second step is surveillance.

For patients with cervical cancer and positive adenopathy and distant metastases based on imaging:

- 1a: Primary treatment is systemic therapy (1) with radiotherapy (a).

- ±1d: With or without (±) individualized radiotherapy (1d).

Sector 6: Primary Therapy Based on Surgical Lymph Node Status (Stage IICp) (Figure 10)

For patients with stage IIC1p cervical cancer with positive pelvic LN but negative para-aortic LN based on surgical LN status:

- 1b: Primary treatment is radiotherapy (1b).
- 1a, b: Radiotherapy (1) with pelvic EBRT (b) and brachytherapy (a) with concurrent chemotherapy.

For patients with stage IIC2p cervical cancer with positive para-aortic LN and negative distant metastasis based on surgical LN status:

- 1b: Primary treatment is radiotherapy (1b).
- 1a, b: Radiotherapy (1) with extended-field EBRT (b) and brachytherapy (a) with concurrent chemotherapy.

For patients with cervical cancer with positive para-aortic LN and positive distant metastasis on imaging but not by biopsy:

- 1b: Primary treatment is radiotherapy (1b).
- 1a, b: Radiotherapy (1) with extended-field EBRT (b) and brachytherapy (a) with concurrent chemotherapy.

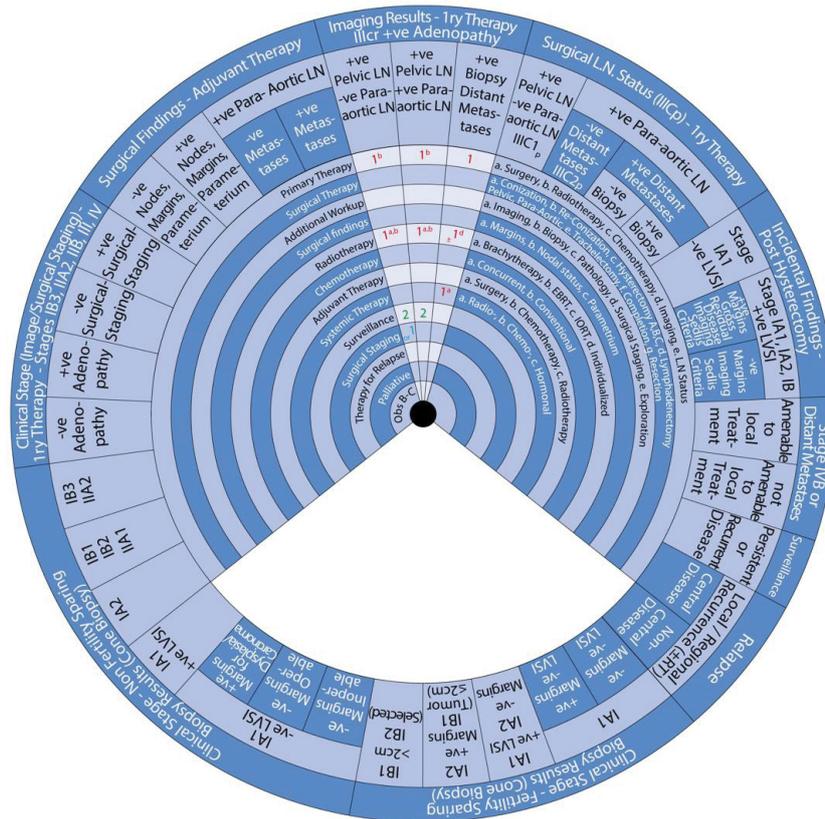


Figure 9: Primary Therapy Based on Imaging Results Demonstrating Positive Adenopathy.

For patients with Stage IIIC2p cervical cancer with positive para-aortic LN and positive distant metastasis on imaging and biopsy:

- 1: Primary treatment is systemic therapy (1).
- ±1d: With or without (±) individualized radiotherapy (1d).

Sector 7: Incidental Surgical Finding of Cervical Cancer Post-Hysterectomy (Figure 11)

For patients with an incidental finding of Stage IA1 cervical cancer with negative LVSI post-hysterectomy:

- 1: Management involves surveillance (1).

| 7.2 Stages IA1, IA2, and IB with Positive LVSI, Negative Margins and Negative Imaging. | |
|--|--|
| 1 ^{ba} | Radiotherapy Pelvic EBRT+ Brachytherapy ± Conc. Chemotherapy |
| or 2 | Or Surgical Therapy Parametrectomy, Vaginectomy + Pelvic Lymphadenectomy ± Para-aortic Lymphadenectomy |
| 2 ^{ba} | Radiotherapy Pelvic EBRT + Brachytherapy ± Conc. Chemotherapy |
| 3 | Observation ^{if} Negative LN and No Residual disease |
| 3 ^b | Radiotherapy Pelvic/Para-aortic EBRT ± Brachytherapy + Conc. Chemotherapy (if Positive LN or Residual disease) |

For patients with an incidental finding of stage IA1, IA2, or IB cervical cancer with positive LVSI but negative margins and negative imaging post-hysterectomy:

- 1b: Primary treatment is radiotherapy (1b).

- 1a, b: Radiotherapy (1) with extended-field EBRT (b) and brachytherapy (a) with or without concurrent chemotherapy.
- or 2: An alternative is a surgical treatment (2) with parametrectomy, vaginectomy, and pelvic lymphadenectomy with or without para-aortic lymphadenectomy.
- or 2b, a: Another alternative is radiotherapy (2) with pelvic EBRT (b) and brachytherapy (a) with or without concurrent chemotherapy.
- 3: The next step is observation (3) if negative LN and no residual disease.
- 3b: The next step is radiotherapy (3) with pelvic/para-aortic EBRT (b) with or without brachytherapy and concurrent chemotherapy if positive LN or residual disease.

For patients with an incidental finding of Stage IA1, IA2, or IB cervical cancer with positive LVSI, margins, and imaging post-hysterectomy:

- 1a: Primary treatment is additional workup with imaging (1a) and further management depends on the findings.

Sector 8: Stage IVB or Distant Metastases (Figure 12)

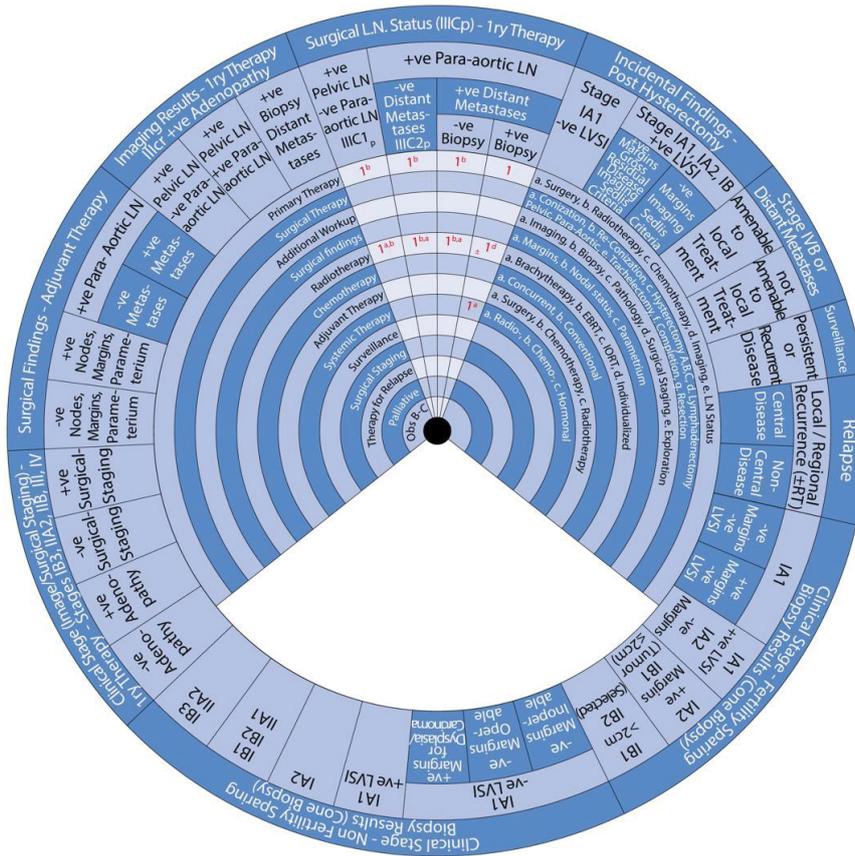


Figure 10: Primary Therapy Based on Surgical Lymph Node Status (Stage IIIc).

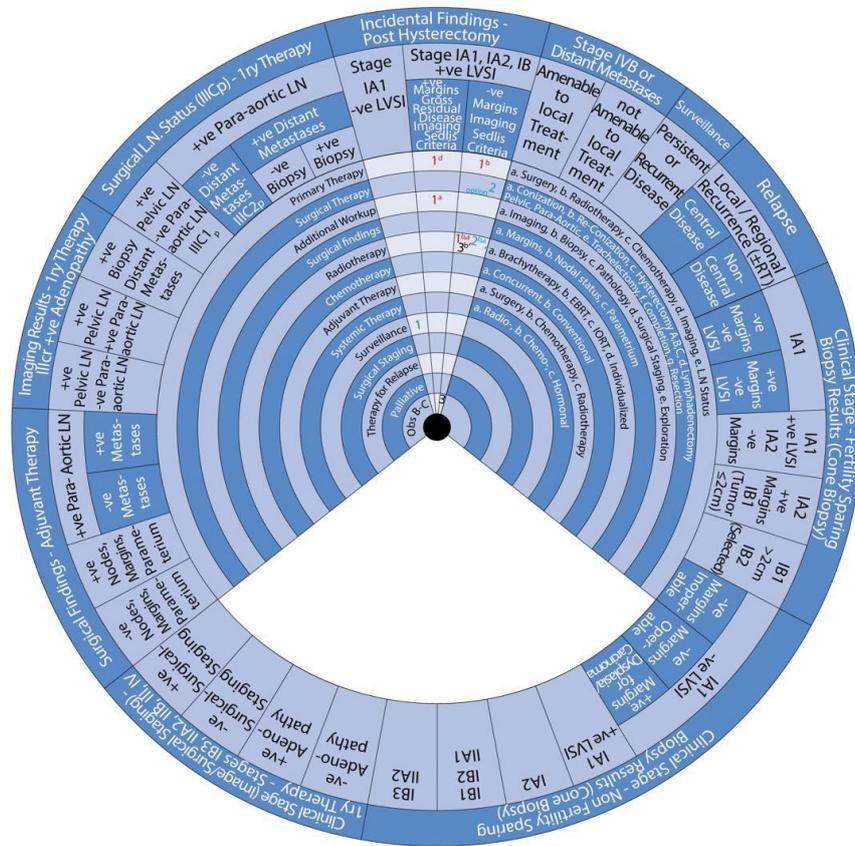


Figure 11: Incidental Surgical Finding of Cervical Cancer Post-Hysterectomy

For patients with stage IVB cervical cancer or distant metastases amenable to local treatment:

- 1g: Primary treatment is surgical resection (1g).
- ±1b: With or without (±) radiotherapy (1) with individualized EBRT (b).
- 1: An alternative is a surgical treatment (1) with local ablation.
- ±1b: With or without (±) radiotherapy (1) with individualized EBRT (b).
- or 1b: Or radiotherapy (1) with individualized EBRT (b) alone.
- ±1: With or without (±) systemic therapy (1).
- #2: Consider (#) adjuvant therapy (2) with systemic therapy.
- 3: The next step is surveillance (3).

For patients with stage IVB cervical cancer or distant metastases not amenable to local treatment:

- 1: Primary treatment is systemic therapy (1).
- or 1: An alternative is supportive care (1).

Sector 9: Surveillance of Persistent or Recurrent Disease (Figure 13)

Surveillance of persistent or recurrent disease involves:

- 1a, e: Primary treatment is additional workup (1) with imaging (a) and surgical exploration (e).
- 1: This is followed by therapy for relapse (1).

Sector 10: Therapy for Relapse (Figure 14)

For patients with local/regional recurrence of cervical cancer with no prior RT:

- #1g: Consider (#) surgical treatment (1) with resection (g).
- 1b, a: An alternative is radiotherapy (1) with individualized EBRT (b) with or without brachytherapy (a).
- ±1: With or without (±) systemic therapy (1).

For patients with central-local/regional recurrence of cervical cancer with prior RT:

- 1f, g: Primary therapy is surgical treatment (1) with pelvic exenteration (f, g).
- ±1c: With or without (±) radiotherapy (1) with IORT (c).
- ±1cC: An alternative is a surgical treatment (1) with RH (cC)

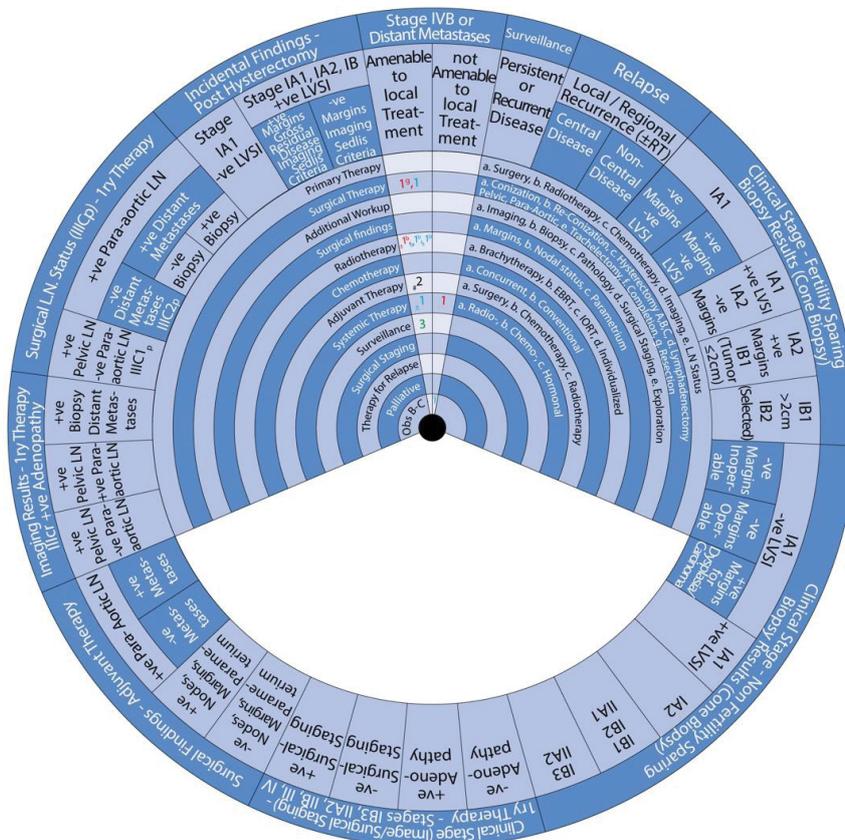


Figure 12: Stage IVB or Distant Metastases.

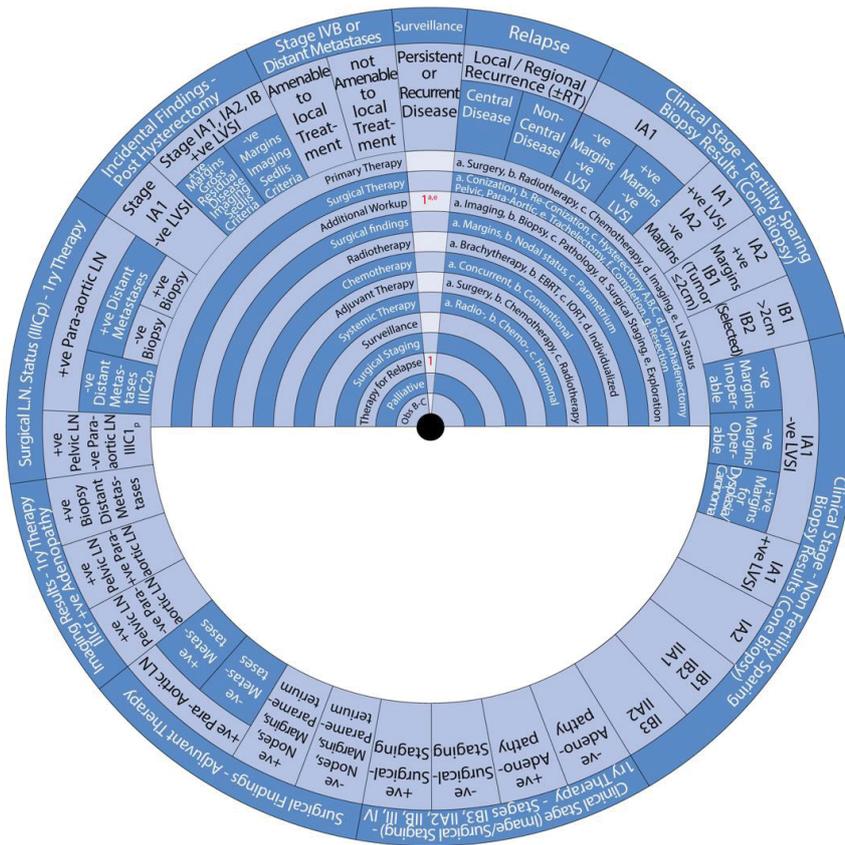


Figure 13: Surveillance of Persistent or Recurrent Disease.

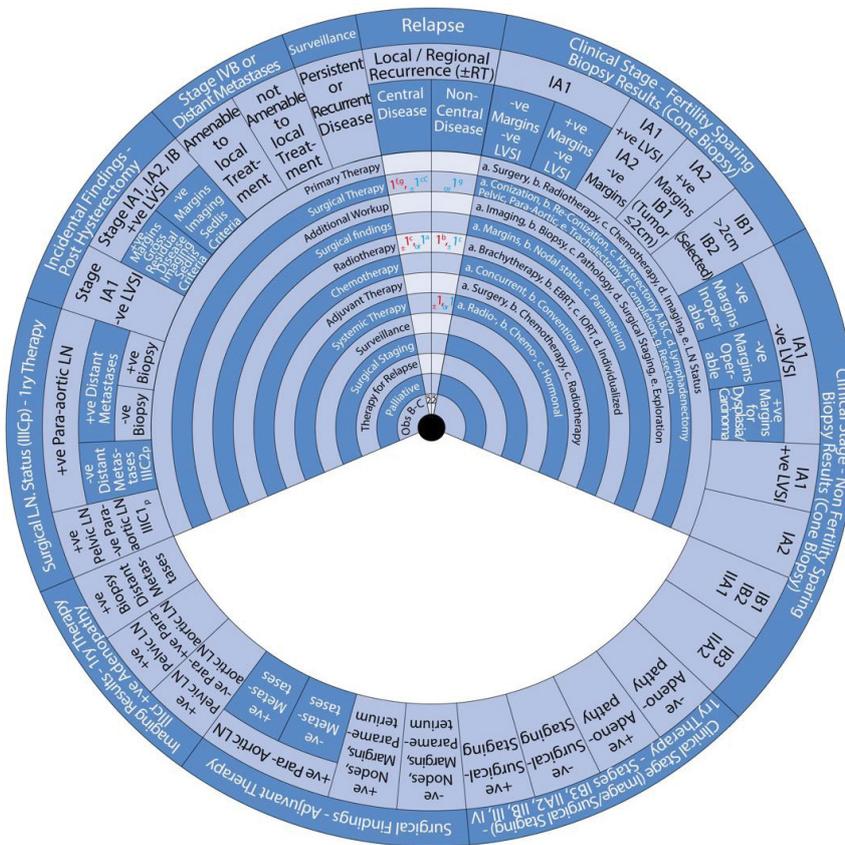


Figure 14: Therapy for Relapse.

- or 1a: Or radiotherapy (1) with brachytherapy (a).
- or 2: Or supportive care.

For patients with non-central local/regional recurrence of cervical cancer and prior RT:

1b: Primary therapy is surgical treatment (1) with pelvic exenteration (f, g).

- ±1: With or without (±) systemic therapy (1).
- or 1g: An alternative is a surgical therapy (1) with resection (g).
- ±1c: With or without (±) alternative is radiotherapy (1) with IORT (c).
- or 1: Another alternative is systemic therapy (1).
- or 2: Or supportive care.

For patients with re-recurrence of cervical cancer:

- 1: Primary therapy is systemic therapy (1).
- or 1: An alternative is supportive care (1).

Discussion

A good staging system allows comparing outcomes of patients with similar characteristics within one center or across multiple centers [6]. Most guidelines including ASCO, BGCS, and NCCN use the FIGO 2018 classification for cervical cancer [1, 4, 6, 7, 9, 10, 17]. Before 2018, FIGO staged cervical cancer mainly based on clinical findings; however, in the recently updated staging system, pathological and imaging findings are taken into consideration [1,6,7]. Guidelines updated before 2018, such as ESGO and ESMO, rely on the Tumors, Nodes, and Metastases (TNM) staging due to this reason [5,13].

Patients with CC must be assessed with a thorough history and examination in addition to laboratory investigations and imaging studies [4,9,10,17,18]. Laboratory investigations include a complete blood count, liver and renal function tests [4,10,18]. Imaging includes chest x-ray, computed tomography (CT), magnetic resonance imaging (MRI) or positron emission tomography/CT (PET/CT) [4,6,9,10,17-19]. MRI is superior to CT in detecting nodal disease but PET/CT is most sensitive [10,19-21]. Pre-operative PET/CT can help detect up to 54.8% of distant metastasis in CC [3].

Surgery is an option for early-stage CC. One option is conization and it aims to achieve negative margins [10,18,20,21]. Another option is hysterectomy, and there are three options: simple, modified radical, and radical [4,7]. Treating early-stage CC with RH and pelvic LND does not preserve fertility [17]. Fertility-sparing treatment is reserved for women with early-stage CC and good prognostic factors with no nodal disease [13,22]. It is not recommended for women with stage IB2 or IIA1 [10,18-20]. LVSI must be ruled out and the tumor has to measure 2 cm or less [10,18]. The presence of LVSI does not affect the staging of CC but it does affect treatment and

the subsequent outcome [10]. Radical trachelectomy entails the resection of the cervix, part of the upper vagina, and the proximal parametria. It is ideally performed in the absence of LVSI, negative margins, and absent nodal disease [22]. Patients need to be counseled on the available treatment modalities and alternatives suitable for their individual case and their risks and benefits [10]. Neoadjuvant chemotherapy can help reduce the size of the tumor prior to surgery and can convert a non-fertility-sparing procedure into a more conservative approach [9,10,18,21].

Sentinel lymph node (SLN) biopsy involves removing the first-draining LNs. SLN biopsy has a high sensitivity in detecting metastasis in tumors measuring 2cm or less. It can be more reliable than LND to determine the nodal status [10]. Adjuvant therapy after surgery is indicated for patients with microscopic margins, nodal disease, and larger tumors [9,10]. It aims to reduce the risk of recurrence and increase the chance of cure [10]. Sedlis criteria can help determine those advised to receive adjuvant therapy as those with high risks including large tumor size, deep stromal invasion, and the presence of LVSI [4,5,7,10,13].

A total dose of radiotherapy administered should be 45-50 Gy [4,10,18,20,21]. Brachytherapy is a key component of RT, especially in patients with Stage IB1 or higher [2,19,20]. Treating women with advanced CC involves RT, including EBRT and BT, and platinum-based chemotherapy [10,20]. Recommended chemotherapy regimens usually include cisplatin with or without paclitaxel with or without bevacizumab [4,5,9,10,17,21]. Adding bevacizumab to the chemotherapy regimen is associated with improved overall survival, with more patients with a complete response without significantly reducing the quality of life [23].

Recurrence can either occur locally or distant and even both [7]. The most common site of recurrence is the pelvis [7,24]. The most common sites for distant metastasis include the lung, para-aortic LNs, and the abdominal cavity [8]. Treatment for recurrence depends on the primary therapy and the location of recurrence [9,10,14,18]. Unlike distant metastases, pelvic recurrences can be potentially cured with pelvic exenteration or radiation [5,8-10,19,21,24]. More than 90% of patients with distant metastasis will die within 5 years. Early-stage CC tends to metastasize locoregionally but can still metastasize to distant sites. Predictors of recurrence include tumor diameter, depth of stromal invasion, and the presence or absence of LVSI. If there is a high risk of recurrence after surgery, then post-operative adjuvant EBRT of the pelvis with or without chemotherapy with or without BT [8].

The aim of surveillance is to detect recurrent disease early when it can be effectively managed [8,13,14]. In a study by Gee et al., 13.7% of patients with locally advanced CC had "unsuspected distant metastases" [3]. The majority of recurrence occurs within 2-3 years after completing treatment and up to 95% of patients are symptomatic on presentation [10,14,18,24]. Follow-up is recommended every 3-4 months for the first two years after completing treatment and every 6-12 months for three more years and then annually or as deemed



appropriate based on the patient's individual risk of recurrence [4,5,9,10,13,14,19-21].

Managing patients with CC requires a multi-disciplinary team, which consists of a gynecologist, gynecologic oncologist, histopathologist, and radiologist, among others [10,13]. It is important to consider that not all patients have access to such services, especially in isolated settings and developing countries. We designed the guide wheel to reflect the recommendations for a highly resourced setting. This wheel is intended to facilitate the referral to established recommendations on managing patients with CC. It is not meant, in any way, to replace algorithms set by the guidelines mentioned. Although this guide wheel was designed during the COVID-19 pandemic, it does not offer any recommendations on changes in practice during this time.

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