



Management of Cervical Cancer in Resource Limited Settings

Linus Chuang MD



Conflict of Interests

None



- Cervical cancer is the **fourth most common** malignancy in women worldwide
 - **530,000 new cases** per year globally
 - **270,000 deaths** per year globally
- About 85% of worldwide deaths from cervical cancer occur in underdeveloped or developing countries
- Death rate is **18 times higher** for low- and middle- income countries compared to wealthier countries

Setting

Treatment	Basic	Limited	Enhanced	Maximal
Surgery	Simple (extrafascial) hysterectomy or more extensive hysterectomy can be performed*	Modified radical or radical hysterectomy	Capable of performing most major surgeries , including radical hysterectomy, radical trachelectomy,† pelvic and para-aortic LN sampling, and pelvic exenteration † Following are not available: PET scan, interventional radiology, sentinel node biopsy/IORT, or bevacizumab	Radical hysterectomy, radical trachelectomy, pelvic and para-aortic LN sampling, sentinel node biopsy , and pelvic exenteration; RT, chemotherapy, interventional radiology, palliative care service, and bevacizumab are all available
Chemotherapy	Availability of chemotherapy drugs is unpredictable	Chemotherapy may be available	Chemotherapy available; bevacizumab not available	Chemotherapy available; bevacizumab is available
RT	No RT available	Limited external RT with no brachytherapy available; in some areas where there is only brachytherapy and no external RT, this will be considered as basic level	RT including external beam and brachytherapy available; interventional radiology not available	RT including external beam and brachytherapy available; interventional radiology available
Pathology	Pathology services are not available; if there is a way to send pathology for review when needed, that should occur (Basic pathology may be available, but diagnosis is often delayed for more than 1 month; there are no frozen sections or pathology consultations in the region)	Pathology services in development (There are basic pathology and frozen section services; consultations are not readily available)	Pathology services in development or not always available (Pathology services including frozen sections are available; tumor registry and regular multidisciplinary conferences are not consistently available in the region)	Pathology available (Full pathology services including diagnosis, consultation, tumor registry, and multidisciplinary conferences are available)
Palliative care	Palliative care service is in development; basic palliative care, including pain and symptom management, should be provided‡	Pain and symptom management available; palliative care service is in development	Palliative care service not always available	Palliative care service available



ASCO Guideline recommendations

- **Basic settings:**
 - **Stage IA:** Cone biopsy if follow-up available
 - **Stage IB1-IVA:** If radiation (RT) unavailable, extrafascial hysterectomy either alone or after chemotherapy
 - **Larger tumors or advanced stage:** neoadjuvant chemotherapy recommended to shrink tumor pre-op
 - **Stage IVB or recurrent cancer:** single agent chemotherapy with cisplatin or carboplatin or palliative care
- **Limited settings:**
 - **Stage IA:** cone biopsy ± PLND (pelvic lymph node dissection)
 - **Stage IB1:** radical hysterectomy plus PLND or radical hysterectomy with adjuvant RT or RT with concurrent low-dose chemotherapy if needed



ASCO Guideline recommendations

- **Limited settings (cont'd):**
 - **IB2-IIA2:** ChemoRT or RT + extrafascial hysterectomy or neoadjuvant chemo + radical hysterectomy
 - **IIB-IVA:** ChemoRT or RT followed by extrafascial/radical hysterectomy \pm PLND \pm PANB (para-aortic node biopsy)
 - **IVB:** Palliative chemotherapy \pm RT of palliative care
- **Enhanced/Maximal Settings:**
 - **IA:** Cone biopsy or extrafascial hysterectomy \pm PLND \pm PANB or pelvic RT with brachytherapy (BT)
 - **IB1:** Radical trachelectomy + PLND or pelvic RT with BT
 - **IB2-IVA:** Pelvic RT + low-dose platinum-based chemo + BT
 - **IVB:** Chemotherapy \pm bevacizumab/palliative care

NACT followed by RH (India) ESMO 2017

- **IB2, IIA, IIB**
 - **633 patients**
 - **3 cycles of paclitaxel (175 mg/m²) and carboplatin (AUC 5-6) every 3 weeks followed by RH vs CCRT**
 - **Primary endpoint: DFS, secondary endpoint: OS**
- **Findings:**
 - **Disease specific DFS: 69.3 vs 76.7% (p = 0.038)**
 - **OS: no differences**
 - **CCRT is superior**
 - **In settings where RT is not available, NACT followed by surgery may still be the best option**



NACT followed by RH (EORTC)

- This is the largest randomized trial in cervical cancer comparing NACT followed by radical hysterectomy with CCRT
- Short term safety is acceptable, mainly due to CT in both arms
- Discontinuation of protocol is high (**20-30%**)
- Pathological complete/ optimal response in NACT - arm = **37%**
- Complete response based on imaging in arm 2 = **49%**
- Adjuvant therapy in arm 1 for patients who underwent surgery = **27%**
- Survival data will follow **mid 2019**



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Guideline implications

- Concurrent RT and chemo is standard in **enhanced and maximal settings** for women with locally advanced disease
- Optimize use of resources
- Low-dose, platinum-based chemo is important during RT, but not at the cost of delaying RT if chemo is not available
- When resources are constrained, clinicians may use fewer fractions of RT with higher dose per fraction, with retreatments if feasible



Guideline implications

- In **limited resource settings** where brachytherapy is unavailable, total dose of EBRT could be used to 68-70 Gy. If residual central disease persists in pelvis at 2 months after treatment completion, surgery to remove residual disease is an option
- In **basic settings** where patients cannot receive RT, extrafascial hysterectomy alone or after chemo may be an option for women with IA1-IVA disease
- For disease with **low likelihood of cure palliative care** should be considered



Summary

- There were no literature to inform practice in the basic setting.
- For a patient who has early-stage disease (stage IA2, IB1, or IIA1), if the surgeon can remove the tumor safely, with negative margins, the Expert Panel recommends performing extrafascial hysterectomy in basic setting.
- For women with larger tumor (IB2 or greater), the Expert Panel recommends NACT whenever chemotherapy is available, for the purpose of shrinking the tumor before performing hysterectomy in basic setting.
- The specific chemotherapy may be carboplatin, cisplatin, or paclitaxel plus carboplatin.
- Extrafascial hysterectomy may be used for patients with stage IB2 or IIA2 to IIIA disease after NACT when appropriate.



Summary

- When resources are **available**, the standard treatment for locally advanced cervical cancers is concurrent chemoradiotherapy with platinum-based chemotherapy, with RT consisting of EBRT with BT and use of extended field RT if para-aortic or common iliac node positive disease
- In **limited** settings, when brachytherapy is **unavailable**, patients may receive neoadjuvant chemoradiotherapy/RT with extrafascial/radical hysterectomy or neoadjuvant chemotherapy with radical hysterectomy and pelvic lymph node dissection ± para-aortic node biopsy
- In **basic** settings, patients may be treated with platinum-based chemotherapy or receive palliative care

Gynecologic Cancer InterGroup
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Thank you!

Cervix Cancer Education Symposium, February 2018

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Management and Care of Women with Invasive Cervical Cancer: Case Study of an Operable Case



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Cervix Cancer Education Symposium, February 2018



Case presentation

A 35-year-old woman complains of postcoital spotting over the past 6 months. She has smoked 1 pack per day for 15 years.

On examination, her back examination shows absence of costo-vertebral angle tenderness. The speculum examination reveals a **5-cm exophytic lesion involving the anterior and posterior lip of the cervix.**



Next step

1. Biopsy of the cervical lesion.
2. Complete blood count.
3. Liver and renal functions tests.
4. Chest x-ray.
5. Smoking cessation and counseling: may offer for HIV testing.
6. CT scan of the abdomen and pelvis. (Limited)



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Cervical biopsy reported as squamous cell carcinoma. The remaining of the work-up were within normal limits. She was staged as IB2.



Clinical approaches

- 1.If chemotherapy is not available, extrafascial hysterectomy (modification as deemed necessary) may be performed if the surgical capacity is present. **(Basic)**
- 2.If chemotherapy is available, neoadjuvant chemotherapy (NACT) followed by radical hysterectomy. **(Basic/Limited)**
- 3.If external beam radiotherapy (EBRT) is available, but not brachytherapy, then chemoRT followed by extrafascial hysterectomy or RT (if chemotherapy not available) followed by extrafascial hysterectomy. **(Limited)**
- 4.If no EBRT is available, then brachytherapy and concurrent low-dose platinum-based chemotherapy followed by radical hysterectomy. **(Limited)**
- 5.Radical hysterectomy plus pelvic lymphadenectomy (PLND) \pm para-aortic LN sampling. **(Limited)**

Note: With risk factors (Sedlis' criteria) on pathology specimen: adjuvant RT \pm chemotherapy after hysterectomy. (Evidence: low/Recommendation: weak)

Treatment course

The patient and her family was counseled on options of management of her stage IB2 squamous cell carcinoma of cervix which included neoadjuvant chemotherapy followed by radical hysterectomy or chemoradiation therapy followed by extrafascial hysterectomy because of the **lack of brachytherapy**. Cisplatin was not available at the time she began her radiation therapy. She underwent 50 Gy external beam radiation therapy and an external beam boost to a dose of 68 Gy. A 1 cm residual tumor was noted at 5 weeks after completion of CCRT. Extrafascial hysterectomy was performed without any complication. Final pathology reported microscopic residual disease on her final pathology specimen. She was followed up every 6 months with no additional treatment.

Management and Care of Women with Invasive Cervical Cancer: Case Study of an Inoperable Patient

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FACRO, FACR, FASTRO**
Radiation Oncologist
Loyola University
Maywood, IL



Cervix Cancer Education Symposium, February 2018



Case presentation

46 year G6P6 old female presents with vaginal bleeding, pelvic pain, weight loss and fatigue. She has not had routine health care. On examination, her blood pressure is 110/80 mm Hg, temperature is 99F (37.2C), and heart rate is 100 beats per minute. Her heart and lung examinations are within normal limits. The abdomen reveals no masses, ascites, or tenderness. No palpable adenopathy. The pelvic examination reveals normal external female genitalia. The speculum examination reveals a exophytic lesion involving the entire cervix. Bimanual/rectovaginal exam reveals **an 8 cm lesion extending to the right pelvic sidewall and left lateral parametrium.**



Treatment course

- **Basic** setting are recommended to receive **palliative care**
 - If available, may receive **neoadjuvant chemotherapy and extrafascial hysterectomy**
- **Limited** setting:
 - Recommend **RT ± concurrent low-dose platinum chemotherapy followed by brachytherapy**
 - If brachytherapy unavailable, can use an external beam boost up to total dose of 68-70 Gy and/or Neoadjuvant chemoradiotherapy or RT with extrafascial or radical hysterectomy
 - Neoadjuvant chemotherapy with radical hysterectomy and pelvic lymph node dissection ± para-aortic node biopsy



Progression

- **Basic** setting:
 - **Palliative care**
- **Limited** setting:
 - Depends on previous receipt of RT and location of failure relative to previously treated field
 - **Tumor-directed RT**
 - **Platinum-based chemotherapy**
 - If no previous RT due to prior resource availability limitations, treat with concurrent chemoradiation with platinum-based chemotherapy

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