Cervical Cancer – Loco-regional recurrence after Previous Radiotherapy

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Recurrent Cervical cancer

• Pelvic recurrences after initial treatment for Cervical cancer typically present within 24-36 months after treatment
• Incidence of pelvic recurrence after initial treatment:
  – 5-15% in Stage 1B-IIA
  – 20-45% in stage IIIB-III
• Prognosis after recurrence: 3-13%
Recurrent Cervical cancer

• Risk factors for recurrence:
  – Nodal involvement
  – Tumour size
  – Depth of stromal invasion
  – Vascular invasion
  – Corpus invasion
Cervical Cancer

THERAPY FOR RELAPSE

Local/Regional recurrence

Prior RT

Noncentral disease

Central disease

Pelvic exenteration
± intraoperative RT (IORT) (category 3 for IORT)

or

In carefully selected patients with small (<2 cm) lesions

Radical hysterectomy
or
Brachytherapy

Tumor-directed RT ± chemotherapy

or

Resection ± IORT (category 3 for IORT)

or

Clinical trial
or
Chemotherapy
or
Best supportive care
(See NCCN Guidelines for Palliative Care)

No prior RT or failure outside of previously treated field
Consider surgical resection, if feasible

Tumor-directed RT + platinum-based chemotherapy ± brachytherapy

Recurrence

Clinical trial
or
Chemotherapy
or
Best supportive care
(See NCCN Guidelines for Palliative Care)

kSee Principles of Radiation Therapy for Cervical Cancer (CERV-B).

Concurrent cisplatin-based chemotherapy with RT utilizes cisplatin as a single agent or cisplatin plus 5-fluorouracil.

See Chemotherapy Regimens for Recurrent or Metastatic Cervical Cancer (CERV-D).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
Radical Hysterectomy

• Small recurrent tumours – Radical hysterectomy:
  – survival rates of 27%-72% possible with high morbidity rates
Pelvic Exenteration

- Pelvic Exenteration is in most cases the only potentially curative treatment option
- Done first in the 1950’s
- Early results – 5 yr OS 20-40% but with peri-operative mortality of 10-26%
- Later results – 5 yr OS 20-70%, operative mortality down to 1-10%
Pelvic Exenteration

• Contraindications:
  – Multiple pelvic and para-aortic nodal metastasis
  – Peritoneal metastasis
  – Distant metastasis
  – Generally not indicated in patients with > stage IIB disease at time of initial diagnosis
Pelvic Exenteration

• Classically 3 types: anterior posterior and total
• Alternative classification:
  type I – Supralevator
  type II – Infralevator
  type III – with vulvectomy
• Pelvic reconstructive surgery
  – urinary divergence (continent/ vs not)
  – Rectal anastomosis
  – Neo-vagina
Pelvic Exenteration

• Prognostic factors:
  – Surgical Margins
  – Nodal status
  – Tumour size
  – DFI: <2 years – 15%, 2-5 years 30%, >5 years 80%
Pelvic Exenteration – In perspective

- UCLA
  - Duration: 45 years
  - Patients: 75
  - Survival: 54% OS

- Albert Einstein College of Medicine
  - Duration: 16 years
  - Patients: 103
  - Survival: 47% OS

- Universality of Michigan
  - Duration: 20 years
  - Patients: 100
  - Survival: 61% OS

- Universitaets Frauenkliniek
  - Duration: 19 years
  - Patients: 203
  - Survival: 21% OS
Surgery for pelvic side wall recurrences

- Hockel proposed laterally extended endopelvic resection (LEER)
  - Includes internal iliac vessels, endopelvic part of the obturator internus, coccygeus, ileococcygeus and pubo-coccygeus muscles
- Mortality 2%, Major Morbidity 70% and 5yr OS 55%
  - (This included primary and recurrent disease)
Neo-adjuvant chemotherapy

- Lopez-Graniel et al: Neo-adjuvant platinum based chemotherapy – 2-4 cycles
- 50% response rate
- MS for responders – 32/12
- MS for non-responders – 3/12
- MS for all – 11/12
  (MS for palliative chemotherapy – 6-10/12)
IORT

• The aim is to increase the pool of potentially operable patients
• Those with disease close to the pelvic side wall, possibly for those with para-aortic nodes
• Monge et al: 31 patients
  – 10 year LCR – 46%
  – 10 year OS – 10%
IORT

- Gemignani et al: 17 patients, IORT – 14Gy
  - 3 yr LCR – 67% (Complete excision - 83%
    Incomplete excision – 25%
  - GI obstruction – 24%
  - Wound complications – 24%
  - Peripheral neuropathy – 18%
  - RVF – 12%
  - Ureteral obstruction – 12%
IORT
IORT
Salvage radiotherapy

• Does it make sense?
Salvage radiotherapy

1. Failed modality

2. Increased morbidity
Brachytherapy as salvage therapy

- Danish K et al: 22 patients, median dose 25Gy
  - Median survival – 9.2 months
  - CR – 22.3%
  - Factors influencing outcome;
    - Primary stage of disease II>III
    - Amount of parametrial infiltration
    - Time from initial treatment - more or less than 24 months
  - Grade IV toxicity – 18%
  - Mortality – 0%
Brachytherapy as salvage therapy

- Mabuchi et al: 52 patients
  - Local CR: 76.9% at 32 months
  - Grade III-IV toxicity – 25%
Brachytherapy as salvage therapy

• Zolciak-Siwinska et al: 20 patients
  – 3 year OS 68%
  – 3 year DFS 42%
  – 3 year LC 45%
  – Grade II toxicity – 15%
  – Prognostic factors:
    • Tumour diameter: 3cm
    • Time to relapse: 12 months
Stereotactically Body Radiotherapy

- Concept of stereotactic radiosurgery was first devised and used for cranial tumours
- It entails:
  - Stereotactic localization
  - Excellent target delineation
  - Tight margins
  - Steep dose curve
  - Reproducibility
SBRT

• Dewas et al: 16 patients with lateral pelvic wall recurrences
  – 4 patients – Gynaecological tumours
  – 1 year LC – 51.4%
  – ? Impact on OS
SBRT

• Gluckenberger et al: 19 patients
  – LCR – 100% (FU of 8-18 months)
  – No acute toxicity, but one patient developed ileus at 18 months
SBRT

• Deodato et al: 11 patients
  – 2 year Local DFS 81%
  – 2 year metastasis free survival – 54%
Gamma knife

GAMMA KNIFE MACHINE
How it works

The patient's head is enclosed in a helmet device which focuses narrow beams of gamma radiation to target a tumour in the brain.
Cyber knife
Linear accelerator
Conclusion

• Local relapse after initial treatment for cervical carcinoma is problematic with relatively poor outcomes
• Data is limited
• In general the preferred treatment after failed radiotherapy is surgery
• Few patients are eligible for surgery and a significant proportion of these are found to be inoperable at time of surgery
• Radiotherapy as an adjuvant to surgery may be beneficial
Conclusion

• Re-irradiation is an option, but it should make sense
• If re-irradiation is considered the volume of treatment should be minimized and the dose to normal tissue limited
• Various techniques and technologies are available – IMRT, VMAT, SBRT, Brachytherapy
Conclusion

• One of the most important factors is the time to relapse

• *There is no reason not to consider standard re-irradiation in patients with a long DFI*
Best Management for Recurrent disease?
Prevention!