Late effects of treatment, including Lymphedema Radiotherapy

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Primary radiochemotherapy in cervical cancer

External beam radiotherapy and concurrent chemotherapy

Start

45 Gy

Cisplatin 40 mg/m²

1 Cycle

5-6 Cycles

Week 1
Week 2
Week 3
Week 4
Week 5
Week 6

Brachytherapy

HDR or PDR

EVD₂ 60 Gy
EVD₂ 85 Gy

Week 1
Week 2
Week 3
Week 4
Week 5
Week 6

5-7 weeks of treatment with external therapy, chemotherapy and intracavitary (internal) radiation
Applicator insertion

Intracavitary (internal) radiation done in anesthesia, is essential for treatment.
MRI guided Brachytherapy in a FIGO stage IV A cervical cancer patient

Modern radiation techniques improve normal organ sparing and decrease side effects.
Image-guided adaptive Brachytherapy

- Repetitive Imaging diagnosis, EBRT/ChT
- Repetitive clin exam +3D/4D drawing
- Applicator insertion
- 3D/4D imaging: applicator in place
- Contouring
- Applicator Reconstruction
- 3D dose planning
- Dose delivery
Modern techniques result in very good tumour control and survival.

RetroEMBRACE: Outcome

Pattern of Relapse

Sturdza et al. Radiotherapy Oncology, 2016
Late side effects

• Can occur at any time after the completion of treatment

• Are more frequent in locally advanced cancers treated with curative intent (i.e. cervical cancer)

• In severe cases may require treatment/intervention

• Many could be prevented through appropriate supportive care
**Overview: Gastro-intestinal**

-maximum incidence of individual bowel symptoms

<table>
<thead>
<tr>
<th>CTCAE 3.0</th>
<th>Diarrhea</th>
<th>Flatulence</th>
<th>Incontinence</th>
<th>Stenosis</th>
<th>Fistula</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade 0</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1023 (95%)</td>
<td>992 (92%)</td>
<td>1066 (99%)</td>
<td>1078 (99%)</td>
<td>1077 (99%)</td>
</tr>
<tr>
<td>Max FUP</td>
<td>568 (58%)</td>
<td>592 (61%)</td>
<td>840 (86%)</td>
<td>947 (98%)</td>
<td>963 (99%)</td>
</tr>
<tr>
<td><strong>Grade 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>48 (5%)</td>
<td>70 (7%)</td>
<td>13 (1%)</td>
<td>1 (0.01%)</td>
<td>2 (0.02%)</td>
</tr>
<tr>
<td>Max FUP</td>
<td>319 (33%)</td>
<td>299 (31%)</td>
<td>108 (11%)</td>
<td>11 (1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td><strong>Grade 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>7 (0.6%)</td>
<td>17 (2%)</td>
<td>0</td>
<td>4 (0.4%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Max FUP</td>
<td>71 (7%)</td>
<td>81 (8%)</td>
<td>20 (2%)</td>
<td>4 (0.4%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td><strong>Grade ≥3</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1 (0.1%)</td>
<td>0</td>
<td>0</td>
<td>10 (1%)</td>
<td>6 (0.6%)</td>
</tr>
<tr>
<td>Max FUP</td>
<td>14 (1%)</td>
<td>4 (0.4%)</td>
<td>0</td>
<td>10 (1%)</td>
<td>6 (0.6%)</td>
</tr>
</tbody>
</table>

* G1 morbidity increases significantly compared to baseline

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Diarrhea, bloating, fecal urgency and incontinence occur to some degree in 1/3 of patients, but severe side effects happen in less than 2%.

*Jensen et al, ESTRO 2017*
## Bladder and urinary toxicity

**970 patients**

<table>
<thead>
<tr>
<th></th>
<th>Frequency</th>
<th>Incontinence</th>
<th>Spasm</th>
<th>Bladder contracture</th>
<th>Ureter stenosis</th>
<th>Cystitis</th>
<th>Bleeding</th>
<th>Fistula</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>G0</strong></td>
<td>482 (47.7%)</td>
<td>643 (66.3%)</td>
<td>898 (97.9%)</td>
<td>964 (92.6%)</td>
<td>930 (95.9%)</td>
<td>797 (82.2%)</td>
<td>916 (94.4%)</td>
<td>957 (98.7%)</td>
</tr>
<tr>
<td><strong>G1</strong></td>
<td>378 (30.0%)</td>
<td>225 (23.2%)</td>
<td>58 (6.0%)</td>
<td>58 (6.0%)</td>
<td>10 (1.0%)</td>
<td>109 (11.2%)</td>
<td>41 (4.2%)</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td><strong>G2</strong></td>
<td>96 (9.9%)</td>
<td>86 (8.9%)</td>
<td>13 (1.3%)</td>
<td>13 (1.3%)</td>
<td>9 (0.9%)</td>
<td>57 (5.9%)</td>
<td>11 (1.1%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td><strong>G3</strong></td>
<td>14 (1.4%)</td>
<td>12 (1.2%)</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
<td>18 (1.9%)</td>
<td>5 (0.6%)</td>
<td>2 (0.2%)</td>
<td>5 (0.5%)</td>
</tr>
<tr>
<td><strong>G4</strong></td>
<td>4 (0.4%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>3 (0.3%)</td>
<td>1 (0.1%)</td>
<td>0 (0%)</td>
<td>3 (0.3%)</td>
<td></td>
</tr>
</tbody>
</table>

* 7 patients had tumor involvement of the bladder at time of diagnosis

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**Frequency, painful urination, cystitis and incontinence occur to some degree in 1/3 of patients, but severe side effects happen in less than 2%**

Fokdal et al, 2016
# Vaginal symptoms

<table>
<thead>
<tr>
<th></th>
<th>N=767</th>
<th>Vaginal dryness</th>
<th>Vaginal stenosis</th>
<th>Vaginal mucositis</th>
<th>Vaginal bleeding</th>
<th>Vaginal fistula</th>
<th>Other vag. symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>G0</td>
<td>767</td>
<td>395 (51%)</td>
<td>287 (37%)</td>
<td>529 (69%)</td>
<td>498 (65%)</td>
<td>753 (98%)</td>
<td>671 (88%)</td>
</tr>
<tr>
<td>G1</td>
<td>767</td>
<td>328 (43%)</td>
<td>339 (44%)</td>
<td>199 (26%)</td>
<td>259 (34%)</td>
<td>5 (1%)</td>
<td>74 (10%)</td>
</tr>
<tr>
<td>G2</td>
<td>767</td>
<td>44 (6%)</td>
<td>128 (17%)</td>
<td>33 (4%)</td>
<td>9 (1%)</td>
<td>1 (1%)</td>
<td>17 (2%)</td>
</tr>
<tr>
<td>G3</td>
<td>767</td>
<td></td>
<td></td>
<td>12 (2%)</td>
<td>5 (1%)</td>
<td>5* (1%)</td>
<td>4</td>
</tr>
<tr>
<td>G4</td>
<td>767</td>
<td></td>
<td></td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td>1* (1%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Vaginal dryness, narrowing, painful intercourse, discharge occur to some degree in 1/2 of patients, but severe side effects happen in less than 4%.

* 2 vesico-vaginal
  1 uretero-vaginal
  1 recto-vaginal
  2 vesico+recto-vaginal

Courtesy of Kathrin Kirchheiner, 2017
Lymphedema

- Lymphedema is a collection of fluid that causes swelling in the arms and legs.
- Without normal lymph drainage, fluid can build up in the affected arm or leg, and lymphedema can develop.
- Medication such as Tamoxifen, radiation therapy, surgery and injury to the lymph nodes can also cause lymphedema.
Lymphedema is the consequence of inappropriate lymphatic drainage.
**Frequency of Lymphoedema**

1176 pts, FU 27 months

**Physician assessed limb edema (CTCAE)**

- G4
- G3
- G2
- G1
- G0

N= 1175 1135 1011 901 868 665 524 365 326 190

**Patient reported limb edema (EORTC)**

- very much
- quite a bit
- a little
- not at all

Progressive manifestation pattern over time

*Najjari D. & al, ESTRO 2017*
Severe and moderate lymphedema occurs very rarely (5%) significantly increased by preexisting comorbidities, higher body mass index, invasive lymph node staging, previous abdominal/inguinal surgery and extended radiation fields.
Side effects of Radiation: Human factor

Kirchheiner et al/Gynecologic Oncology, 2015
Psychosocial consequences of cancer treatment are transient and QoL improves after a while in the majority of patients.
Conclusion

- Radiation treatment of gynecologic cancer can cause long-term side effects impacting to some degree on the quality of life of patients.

- While 1/3 to ½ of patients may develop some kind of long-term toxicity, severe toxicity is very rare.

- In some gynecological malignancies, the benefit of Radiation treatment may outweigh the limited toxicity (i.e. Cervical cancer).

- Future research is aiming to improve the outcome while decreasing the toxicity profile.
Conclusion: multidisciplinary team work is needed

Thank you!

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