Organ preservation in rectal cancer

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• No disclosures
Major steps forward

• Surgical technique: TME +++

• Radiotherapy +

• Imaging: MRI ++

• Minimal invasive techn. +

• Systemic therapy +/-
20-30 yrs randomized trials
(Ch)RT and TME Surgery
Goal: improving oncological results

Better local control
No survival advantage
Functional disadvantage
Improved outcome?

- Postop morbidity – mortality
- Frail – Elderly
  - goal: remaining independent?
- Anorectal/urogenital function
- Body image
- Patient preference
Organ preservation

Prospective studies small tumors – TEM
Observational studies complete responders
Goal: improving functional results

Good functional results
Local tumor control?
Neoadjuvant ChRT and TEM

• T1, T2, small T3, usually N0
• ChRT and TEM of remaining scar/tumor
• Completion TME when >pT1, incomplete, …

• Organ preservation in 50-60%
• ypT0 in around 50%
Neoadjuvant ChRT and TEM

• Works well for small tumors
  – High chance of organ preservation
  – Beneficial for the good responders

• Dilemma: those who still require a TME?
  – Double toxicity of ChRT and surgery?
  – Would have been better off with surgery only?
STAR TREC

- cT1-3N0 <4cm
  - Radical Surgery
  - Organ preservation
    - 5x5 Gy
    - evaluation
      - cCR
      - near cCR
      - no response
    - Organ preservation
      - CRT
      - W&W
      - TEM
      - TME

week 1-5
TME
week 11-13
week 13-15

DUTCH CANCER SOCIETY
Small tumours
- additional ChRT
- ‘planned’ organ pres.
- +/- local excision

>50% 10-25%

Large tumours
- Standard ChRT + TME
- ‘opportunistic’ organ pres.
- W&W

Organ Preservation
Watch & Wait

Operative Versus Nonoperative Treatment for Stage 0 Distal Rectal Cancer Following Chemoradiation Therapy
Long-term Results

Journal of Clinical Oncology

Wait-and-See Policy for Clinical Complete Response After Chemoradiation for Rectal Cancer

Original Article

Watch-and-wait approach versus surgical resection after chemoradiotherapy for patients with rectal cancer (the OnCoRe project): a propensity-score matched cohort analysis

Original Report

High-dose chemoradiotherapy and watchful waiting for distal rectal cancer: a prospective observational study

Long-term Outcome of an Organ Preservation Program After Neoadjuvant Treatment for Rectal Cancer

Netherlands Cancer Institute
Antoni van Leeuwenhoek
2004: My first W&W patient

- age 67, distal cT3N1M0
- plan: chemoradiation and APR
- refused surgery
Protocol

Rectal Ca → CRT → 10 week interval

- residual tumor → TME
- cCR → W&S
- 'near cCR' → TEM
Are you sure the tumour is completely gone?
Selection of patients

Shared decision making:
risk – benefits - uncertainties
STANDARD MRI
DIFFUSION MRI
tumor
Complete response
Selection cCR Endoscopy or DWI?

AUC 0.91

Source of the Curve
- T2
- DWI + T2
- Endoscopy
- Endo + DWI + T2
- Reference Line

Maas et al. Annals Surg Oncol 2015
Follow up

• Selection of complete response
  – Not 100% accuracy

• Acceptable if
  – Persistence of tumour detected early
  – Salvage treatment is successful

• Change of concept
Follow-up

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
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<tbody>
<tr>
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<tr>
<td>4x Endoscopy</td>
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Patients 2004-2018

- 354 patients
- Stage III: 71%
- Distal tumors: 77%
- 93% after chemoradiation
- 7% after 5x5Gy long interval (chemo)
- Estimated 15% of CRT patients
Oncological outcome
mean follow up: 28 months

354 cCR

326 W&S

52 LR
3 NR
3 L/NR
7 Met

96% survival

14pCR

2 Met

93% survival

28 TEM

11 ypT2

4 LR
1 NR
1 L/NR
1 Met

93% survival

3 ypT1
Luminal – nodal regrowth
Small luminal recurrence

ypT2N0

6 m

11 m

15 m

22 m
Oncological outcome

- all regrowth < 2 years
- completion/salvage surgery in all patients
- 100% pelvic control
- no M+ originating from regrowth (?)
Follow up!!
High presacral extramural recurrence
Functional outcome

- 3 yr colostomy free rate >90%
- EORTC CR38
  - Better in most domains
- LARS
Current protocol – near cCR

- CRT → 10 week interval
- residual tumor → TME
- cCR → W&W
- ‘near cCR’ → TEM

“Test of time”
Time heals

8 weeks: flat ulcer – no Bx

16 weeks: flat ulcer – no Bx
Organ Preservation
Very high interest of patients
Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWDD): an international multicentre registry study


Lancet 2018

- 42 centers: 880 pts cCR, median FU 3.4 yrs
- Local regrowth rate 24%  (97% endoluminally)
- Overall Survival 3yr: 93.2%
- Cause of death: rectal cancer 33%
Multi-center registration/implementation
Wait-and-see

- Prospective national study
- Regional expert centers
  - Training-supervision
- All data prospectively entered in database
Can we improve the response rate?

- Systemic therapy
- Radiosensitizers
- Immunotherapy
- Additional radiotherapy
  - External boost
  - Internal: brachy - contact

Appelt 2015 Lancet Oncology

Appelt 2013 IJROBP
Prediction of response

• No single reliable predictive factor
• Multiparameter predictive models will improve
  – Clinical - Biomarkers from biopsy - Radiomics

– Patient A: 70% chance CR -> ChRT
– Patient B: 15% chance CR -> surgery
Organ Preservation - W&W

- Feasible
- Larger tumors: 15-20%
- Smaller tumors: 50%
- With good selection/follow up
  - Local regrowth 15-20%
  - Early detection regrowth – salvage
- No apparent influence on survival (?)
- High interest of patients
Organ Preservation