Surgery for rectal cancer locally advanced

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Actual treatment in rectal cancer

Early rectal cancer (T1,T2,N0)
- T1sm1,(sm2)
- TEM/TAE

Advanced rectal cancer ≥ T3, TxF1
- Neoadjuvant (chemo)radiotherapy
- Radical Surgery
  - TME +/- proctectomy
  - cCR

“wait and see”
organ sparing
Beyond cTNM adverse MRI features

1. Deep mesorectal invasion
2. Involved MRF
3. EMV invasion

T3
distal
N+, EMVI+
T3 > 5mm
CRM+
T3a
mid proximal
Risk profile

Local failure
  low risk  high risk

Distant failure
  low risk  high risk

T3a mid proximal

T3 distal

T3 > 5mm CRM +

N+, EMVI +
Risk profile

Local failure
- low risk → high risk

Distant failure
- low risk → high risk

Primary Surgery

T3a
- mid proximal

T3
- distal

T3 > 5mm CRM +

N+, EMVI +

Chemoradiation

Systemic therapy
EMVI is a poor prognostic factor
EMVI is a poor prognostic factor
MRI risk prediction for pCRM + *Mercury 2*

<table>
<thead>
<tr>
<th>EMVI</th>
<th>Anterior</th>
<th>MRI SAFE &gt; 1mm</th>
<th>MRI UNSAFE</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>≥ 4 cm &lt; 4 cm</td>
<td>≥ 4 cm &lt; 4 cm</td>
</tr>
<tr>
<td>neg</td>
<td>neg</td>
<td>1 4</td>
<td>4 13</td>
</tr>
<tr>
<td>neg</td>
<td>positive</td>
<td>3 10</td>
<td>11 29</td>
</tr>
<tr>
<td>positive</td>
<td>neg</td>
<td>4 13</td>
<td>14 35</td>
</tr>
<tr>
<td>positive</td>
<td>positive</td>
<td>11 30</td>
<td>31 60</td>
</tr>
</tbody>
</table>

Validates the MRI low resection plane assessment
- avoids overuse of neoadjuvant treatment
- need for reassessment after neoadjuvant treatment

Response assessment becomes integrated part of surgical decision making

- Upfront surgery

- Neoadjuvant chemo/rad $\rightarrow$ MR – response assessment

  (flexible interval)

  cCR

  Non-operative

  adapted Surgery
Watch and wait in cCR in locally advanced rectal cancer

- Reduced likelihood for cCR
- Significant regrowth rate

Habr Gama, *Dis Colon Rectum* 2017
What is wrong with RT in low risk rectal cancer

- no survival benefit
- morbidity: acute and late toxicity

- increased risk for LARS, genitourinary dysfunction
- chronic pelvic sepsis
Long-term outcome Dutch TME trial

Lancet Oncol 2012
Surgical decision making in distal rectal cancer = complex

1. Type and extent of primary tumor

2. **Response to chemo-radiation**

3. Perceived ability to clear all tumor (adequate margins)
   - DRM / CRM

4. Patient related factors (functional status, comorbidity)

5. Patients preference
   - acceptance suboptimal functional outcome
Increasing SPS for rectal cancer but large hospital variability: 26.9% - 77% (NCCN)
Large variability of sphincter preserving surgery in distal Rectal Cancer
PROCARE database

1995 – 1997

50 %

2006 – 2009

22 %

APR rate 17% - 85%

low rectal cancer
No difference in oncologic outcome between CAA vs APR

Survival relates to

- poor prognostic factors (tumor specific)
- patient related factors

Not technique related
Can we safely reduce the DRM

2 cm → 1 cm → < 1 cm  
close shave

Distal IM spread after chemoradiation: 2% and all <1cm

IM spread distal to macroscopic margin

Caveat: poorly differentiated /signet cell/tumor budding

Guedj N. Human Pathol 2016; 52:164-172
Response to neo-adjuvant chemoradiation

- assess response [(MRI)]
- expand the interval (from 6 w to 12w)
Technical aspects:
- low stapled and Colo-anal anastomosis (CAA)
- Intersphincteric resection: partial ISR – complete ISR
Rullier type I *
mucosal sleeve and colo-anal anastomosis preserves the IAS

Tekkis P. et al. *Colorectal Dis* 2015
*Rulier E et al. *Dis Colon Rectum* 2013; 56*
Rullier type 2
Partial intersphincteric (full-thickness)

Type 2 - tumour 1–2 cm from dentate line

Schiesser et al. Intersphincteric resection 1994
COLOR II trial (non-inferiority phase III) 2004-2010

1044 patients randomised (2:1)
   699 in laparoscopic surgery group
   345 in open surgery group

Locoregional recurrence rate at 3 years: 5.0% in both groups

DFS: 74.8% (laparoscopic) and 70.8% (open)

OS: 86.7% (laparoscopic) and 83.6% (open)

Disease free survival

Overall survival
## Color II trial: short-term

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopy</th>
<th>Open</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td><strong>Duration of surgery</strong></td>
<td>240 (184-300)</td>
<td>188 (150-240)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Conversions</strong></td>
<td>17%</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Blood loss</strong></td>
<td>200 (100-400)</td>
<td>400 (200-700)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>30-day mortality</strong></td>
<td>1%</td>
<td>2%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Overall morbidity</strong></td>
<td>40%</td>
<td>37%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Leak rate</strong></td>
<td>13%</td>
<td>10%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Hospital stay</strong></td>
<td>8.0 (6.0-13.0)</td>
<td>9.0 (7.0-14.0)</td>
<td>&lt;0.36</td>
</tr>
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*Lancet Oncol* 2013
Transanal TME: optimizing the minimally invasive approach
Distal margin in ta-TME: under direct visual control

single stapled vs manual anastomosis in Rullier type I
CRM positivity

- ta TME Registry
- ta TME Veltcamp
- taTME Burke
- taTME Lacy
- ROLLAR robotic
- ROLLAR laparoscopy
- COLOR II
- CLASSIC
Despite optimized minimally invasive surgery and more sphincter preservation, functional impairment rather than the rule:

- mean BM/ day 2.7
- perfect fecal continence: 51.2%
- urgency 18.9%

Factors influencing functional outcome after colo-anal and intersphincteric resection

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.03</td>
<td>0.98 – 1.08</td>
<td>ns</td>
</tr>
<tr>
<td>Gender</td>
<td>1.14</td>
<td>0.37 – 3.52</td>
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</tr>
<tr>
<td>Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-4</td>
<td>1.31</td>
<td>0.44 – 3.95</td>
<td>ns</td>
</tr>
<tr>
<td>Preop RT</td>
<td>3.07</td>
<td>1.05 – 8.89</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Need to improve functional outcome after TME
Understanding LARS

% LARS / time after restoration transit (mo)

Clustering 76%
> 4 BM/day 54%
Urgency 47%
Incomplete evacuation 33%
Nocturnal BM 30%

Ribas Y. et al Int J Colorectal Dis 2017
Major LARS (score > 30)

- 55%: FL, urgency (34%)
- 24%: evacuat dysf (18%)
- 24%: no clinical LARS (43%)

Minor LARS (score 20 - 30)

- 30%: m (6%)
- 24%: no LARS (score < 20)

no LARS (score < 20)
Advanced rectal cancer increased risk for local and distant failure

- deep mesorectal invasion (> 5mm, >T3b)
- threatened CMF (< 1-2 mm), invaded CMF
- nodes +++ (extramesorectal)
- EMVI
- signet cell, ...
Improving local and distant control in advanced rectal cancer

Higher radiation dose
Effective radiation sensitization

Increasing interval to surgery
Neoadjuvant chemotherapy
Effect of adding mFOLFOX6 after neoadjuvant chemoradiation in locally advanced rectal cancer: a multicentre, phase 2 trial

Ileostomy
Radiotherapy (54 gray) infusional 5 FU additional cycles of Folfox

Posterior pelvic exenteration
Radical ‘en bloc’ surgery in T4b = only chance for cure
Male patient: 75 yrs.
Moderate operative risk, ASA 2
well differentiated adenocarcinoma, juxta-anal (Rullier II) cT3a N?, M0
Different strategies

Low risk cancer: **primary surgery**: IS proctectomy + def stoma

Low risk cancer – expects sphincter preservation

- radiochemotherapy and surgery (TME + colo-anal anal anastomosis)
  - but impaired function

- radiochemotherapy and increased interval and watch and wait

if c CR
Locally advanced rectal cancer

- Spectrum with different risk profiles: local and distant requires adapted multimodal treatment strategies

- MRI optimizes TME and radical surgery

- Transanal TME is the next step in the minimally invasive approach

- Functional outcome should be optimised (focus of clinical research)