RECTAL CANCER: DIAGNOSIS, STAGING AND THERAPY

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DECLARATION OF INTEREST

DISCLOSURE

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Others: Executive Board member of ESMO, Chair of Education ESMO, General and Scientific Director INCLIVA, Associate Editor: Annals of Oncology and ESMO Open, Editor in chief: Cancer Treatment Reviews.
OLD APPROACH TO RECTAL CANCER

- Surgical resection
- Pathology assessment and estimation of risk
- Treatment based upon classical TNM factors
- Postoperative concurrent chemoradiation

The concept of TME surgery
Optimal staging by MRI
Pathological assessment of the quality of surgery
Preoperative radiation or chemoradiation
Integration of knowledge in a multidisciplinary team approach
Selection of patients for preoperative therapy
THE CONCEPT OF TOTAL MESORECTAL EXCISION

Excision line (includes mesorectum)

Mesorectum

Tumor
PREOPERATIVE STAGING OF RECTAL CANCER

**CURRENT KEY CONCEPTS WELL DEFINED BY MRI**

- **BOWEL WALL INVASION**
- **REGIONAL LYMPH NODES**
- **DISTANCE TO MESORECTAL FASCIA**
- **SPHINCTER INVOLVEMENT**
- **VENOUS INVASION**
- **DISTANT METASTASIS**
INVOLVEMENT OF MESORECTAL FASCIA
INVOLVEMENT OF PUBORECTAL SPHINCTER
EXTRAMURAL VEIN INVASION
SURGICAL STAGING OF RECTAL CANCER: THE ROLE OF THE PATHOLOGIST

- Bowel wall invasion
- Regional lymph nodes
- Distant metastasis

Current key pathological concepts:

- Macroscopical integrity of mesorectum
- Distance to circumferential resection margin

Staging after preoperative chemoradiation
THE PATHOLOGIST AUDITS SURGICAL SKILLS: DEFINITION OF PLANE OF SURGERY

PATHOLOGIC ASSESSMENT OF TME QUALITY

Nagtegaal et al, J Clin Oncol 2002
MACROSCOPIC ASSESSMENT OF MESORECTAL EXCISION

MACROSCOPIC ASSESSMENT OF MESORECTAL EXCISION

THE PATHOLOGIST AUDITS SURGICAL SKILLS: MACROSCOPIC ASSESSMENT OF MESORECTAL EXCISION

THE ASSESSMENT OF CIRCUMFERENTIAL RESECTION MARGIN
THE ASSESSMENT OF CIRCUMFERENTIAL RESECTION MARGIN
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THE ASSESSMENT OF CIRCUMFERENTIAL RESECTION MARGIN

Circumferential Margin Involvement Is the Crucial Prognostic Factor after Multimodality Treatment in Patients with Locally Advanced Rectal Carcinoma

### THE IMPORTANCE OF MULTIDISCIPLINARY TEAM DISCUSSION:

Total no. Rectal cancer pts 298

- Potentially curative 259 (87%)
  - Palliative cases 39 (13%)
  - Not discussed 62 (24%)
    - Surgery alone 62 (100%)
      - Histological CRM+ve 16/62 (26%)
      - Histological CRM-ve 46/62 (74%)
    - Discussed 197 (76%)
      - Surgery alone (Group 1) 116 (59%)
        - Histological CRM-ve 113/116 (97%)
        - Histological CRM+ve 1/116 (1%)
      - Refused surgery 2/116 (1%)

Preoperative therapy (Group 2 and 3) 81 (41%)

* Burton et al, Br J Cancer 2006; 94:391-397
A MULTIDISCIPLINARY TEAM APPROACH FOR RECTAL CANCER

• Discussion of all new cases before surgery
• Discussion of MRI data
• Selection of patients for preoperative therapy
• Discussion of pathology report, stressing the assessment of the surgical plane and CRM
• Selection for postoperative therapy
• Detailed discussion of any relapse during follow up
• Yearly audits of all activities and results
Systemic Staging: Thorax and abdominal CT
Local Staging: Rectoscopy, Endorectal US, DRE
MRI* has a key role in defining:
- Prediction of CRM involvement
  - Tumor within 1 mm of the mesorectal fascia
  - T3-4 arising from below the level of origin of the levator muscles
- Extramural spread >5mm
- Extramural Vein Invasion
- Peritoneal involvement

* Burton et al, Br J Cancer 2006; 94:391-397
Randomized Phase III Trial of Preoperative vs Postoperative Conventional Fractionation Chemoradiation for Resectable Rectal Cancer

SAUER et al, N Eng J Med, 2004;351:1731

<table>
<thead>
<tr>
<th>ARM</th>
<th>No. PTS</th>
<th>GRADE 3-4 ACUTE DIARRHEA</th>
<th>GRADE 3-4 ANY ACUTE</th>
<th>GRADE 3-4 ANY LONG TERM</th>
</tr>
</thead>
<tbody>
<tr>
<td>PREOP ChRT</td>
<td>405</td>
<td>12%</td>
<td>27%</td>
<td>14%</td>
</tr>
<tr>
<td>POSTOP ChRT</td>
<td>394</td>
<td>18% p = 0.04</td>
<td>40% p = 0.001</td>
<td>24% P =0.001</td>
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PREOPERATIVE CHEMORADIATION HAS SIGNIFICANTLY LESS TOXICITY THAN POSTOPERATIVE CHEMORADIATION
Randomized Phase III Trial of Preoperative vs Postoperative Conventional Fractionation Chemoradiation for Resectable Rectal Cancer

SAUER et al, N Eng J Med, 2004;351:1731

<table>
<thead>
<tr>
<th>ARM</th>
<th>No. PTS</th>
<th>DFS at 5 y</th>
<th>OS at 5 y</th>
<th>DM at 5 y</th>
<th>LR at 5 y</th>
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</thead>
<tbody>
<tr>
<td>PREOP ChRT</td>
<td>405</td>
<td>68%</td>
<td>76%</td>
<td>36%</td>
<td>6%</td>
</tr>
<tr>
<td>POSTOP ChRT</td>
<td>394</td>
<td>65% p:n.s</td>
<td>74% p:n.s</td>
<td>38% p:n.s</td>
<td>13% p:0.006</td>
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PREOPERATIVE CHEMORADIATION INDUCES SIGNIFICANTLY BETTER LOCAL CONTROL THAN POSTOPERATIVE CHEMORADIATION, WITHOUT ANY EFFECT ON OVERALL SURVIVAL
CONVENTIONAL FRACTIONATION CHEMORADIATION INDUCES A HIGHER RATE OF DOWNSTAGING AND pCR THAN SHORT COURSE RADIATION, WITH NO APPARENT BENEFIT IN LOCAL CONTROL, DFS OR SURVIVAL
Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

R. Glynne-Jones¹, L. Wyrwicz², E. Tiret³, G. Brown⁵, C. Rödel⁶, A. Cervantes⁷ & D. Arnold⁸, on behalf of the ESMO Guidelines Committee*
Localized rectal cancer: Selection of patients

<table>
<thead>
<tr>
<th>Risk group</th>
<th>TN substage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very early</td>
<td>cT1 sm1 N0 (on ERUS and MRI)</td>
</tr>
<tr>
<td>Early (Good)</td>
<td>cT1-cT2; cT3a/b if middle or high, N0 (or also cN1 if high), MRF clear, no EMVI</td>
</tr>
<tr>
<td>Intermediate</td>
<td>cT3a/b very low, levators clear, MRF clear or cT3a/b in mid- or high rectum, cN1-2 (not extranodal), no EMVI</td>
</tr>
<tr>
<td>Bad</td>
<td>cT3c/d or very low localisation levators threatened, MRF clear cT3c/d mid-rectum, cN1–N2 (extranodal), EMVI+, limited cT4aN0</td>
</tr>
<tr>
<td>Advanced (Ugly)</td>
<td>cT3 with any MRF involved, any cT4a/b, lateral node+</td>
</tr>
</tbody>
</table>

PREOPERATIVE TREATMENT SELECTION FOR RECTAL CANCER

• Preoperative versus postoperative
• Short versus long course radiation
• Radiation alone or concurrent chemoradiation
• Chemoradiation based upon single agent (5-FU or oral Fluoropyrimidines) versus combination chemotherapy
Intermediate disease
cT3a/b very low, levators clear, MRF clear, cT3a/b in mid- or high rectum, cN1-2 (not extranodal), no EMVI

TME alone or SCPRT/CRT if good quality mesorectal excision cannot be assured

MRI to re-evaluate tumour

‘Watch-and-wait’ may be considered in high-risk patients if cCR achieved with CRT

TME in most cases (plus photographic record of specimen and assessment of TME quality)
Locally advanced disease cT3c/d or very low, levators not threatened, MRF clear cT3c/d mid-rectum, cN1-N2 (extranodal), EMVI+ → SCPRT or CRT → MRI to re-evaluate tumour → 'Watch-and-wait' may be considered in high-risk patients if cCR achieved with CRT → TME (plus photographic record of specimen and assessment of TME quality)

Advanced disease cT3 with any MRF involved, cT4b, levators threatened, lateral node+ → CRT → SCPRT plus FOLFOX and delay to surgery → MRI to re-evaluate tumour → TME (plus photographic record of specimen and assessment of TME quality) → Further surgery if needed due to tumour overgrowth

LONG TERM OUTCOMES FOR RECTAL CANCER PATIENTS AND cCR AFTER NEOADJUVANT TREATMENT WITHOUT SURGERY: “WACHT AND WAIT” LOCAL AND DISTANT RELAPSES AT 5 YEARS

MEDIAN FOLLOW-UP 3.5 YEARS
N: 880

Van der Valk MJM et al. Lancet 2018; 391:2537-2545
LONG TERM OUTCOMES FOR RECTAL CANCER PATIENTS AND cCR AFTER NEOADJUVANT TREATMENT WITHOUT SURGERY OS AND DFS AT 5 YEARS

Van der Valk MJM et al. Lancet 2018; 391:2537-2545
More and better clinical research is needed to improve current results of rectal cancer

Every patient should be treated within an expert multicisciplinary team

Staging with RMI is mandatory. The use of MRI will allow an appropriate selection of patients at risk of CRM +

When indicated, concurrent 5-FU/capecitabine based chemoradiation should be given preoperatively

Short course RT 5x5 Gy as an option

Currently ongoing and future clinical trials should better determine the role of pre- and postoperative chemotherapy
PERIOPERATIVE MANAGEMENT OF RECTAL CANCER: CONCLUSIONS

- MULTIDISCIPLINARY DISCUSSION ESSENTIAL
- DEFINE AIMS OF THERAPY AND OPTIMAL TREATMENT
- SELECTIVE APPROACH ACCORDING TO MRI IF R0 RESECTION IS THE AIM
  - T1-T3a-b. SURGERY ALONE
  - LOW LOCAL RISK: 5X5 RT VS SURGERY ALONE
  - IF MODERATE LOCAL RISK: RT 5x5 VS LONG COURSE CRT
• TREAT ACCORDING TO AIM: R0 RESECTION vs cCR
• IF AIMING AT cCR A MORE INTENSIVE TREATMENT COULD BE JUSTIFIED AS AN EXPERIMENTAL APPROACH
• IN HIGH RISK MRI DEFINED PATIENTS:
  – MESORECTAL FASCIA INVOLVED OR CLOSED, EMVI+, N2, o LATERAL NODES.
  – A MORE INTENSIVE MULTIMODAL APPROACH MAY BE JUSTIFIED
  – TOTAL NEOADJUVANT TREATMENT SHOULD BE CONSIDERED AS EXPERIMENTAL
Thank you