When to take your decision? Before or after nCRT?

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Is it possible to change operative strategy after nCRT in low rectal cancer?
When to take your decision? Before or after nCRT?

Tumor Response After nCRT

Before Treatment

After radiotherapy

At 12 wks follow up

When to assess tumor response?

- Effect of nCRT on tumor is time dependant
- Standardized time to assess tumor response is after 12 weeks

Effect of nCRT in Rectal Cancer
Downstaging and Downsizing

- Primary tumor (T)
- Depth of tumor penetration (yPT)
- Perirectal lymph nodes (yPN)
- Rates of stage III disease
  - Up to 30% achieve complete response

Disease Free Survival

- pCR 83%
- Incomplete Response 65%

Long-term outcome in patients with a pathological complete response after chemoradiation for rectal cancer: a pooled analysis of individual patient data.
Lancet 2010
When to take your decision? Before or after nCRT?

Pathologic Complete Response?

Is it acceptable to submit a patient to a considerably morbid surgery without removing one cancer cell?
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**nCRT & Colorectal or Coloanal anastomosis**

- Increase frequency
- Need of temporary stoma
- Risk of anastomotic leak, stricture...etc
- Morbidity up to 38%
- Fecal incontinence up to 20%
- Impotence (15%) and urinary problems (20%)

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**APR**

Permenant Stoma???

**Bad Healing!!!!**
1- Wait and See after Complete Clinical Response

- No more than whitening of the mucosa, teleangiectasia with mucosal integrity
- No palpable masses or nodules
- No radiological evidence of extra-rectal disease (MRI, PET, CT)

Habr Gama 2010 DCR
Habar Gama Follow-up Protocol

Clinical & radiological (CT, MRI, PET)
Year 1 every 2 months
Year 2 every 3 months
Year 3-5 every 6 months
Start year 6 every year

- Normal
  - Continue wait and see
- abnormal
  - Go for Surgery

When to take your decision? Before or after nCRT?

- Incomplete CR: Immediate surgery
- CCR: Watch & Wait
Habar Gama Results

- 47 patients had initial complete clinical response.
- 8 developed local re-growth within the first 12 months
- 4 patients developed late local recurrences (>12 months of follow-up).
- 35 patients never underwent surgery

Local recurrences after wait and see: Are they salvageable?

Local recurrence after complete clinical response and watch and wait in rectal cancer after neoadjuvant chemoradiation: impact of salvage therapy on local disease control.

Local recurrences after wait and see: Are they salvageable?

- Local recurrence developed in 31% of (90) patients with initial CCR
- Salvage therapy is possible in ≥ 90% of recurrences
  - 94% local disease control
  - 78% organ preservation

Nonoperative Management of Rectal Cancer With Complete Clinical Response After Neoadjuvant Therapy

Annals of Surgery 2012
When to take your decision? Before or after nCRT?

**NOM**

- 32 patients
- 6 local failure
  - of them 3 have distant recurrence
- 81% avoided rectal resection
- Salvage surgery for local recurrence
- No further local recurrence FU 17 ms

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**NOM**

2–year disease free survival
- NOM group 88%
- Rectal resection/pCR group 98%
  
  \[ P = 0.27 \]

**Overall survival**
- NOM group 96%
- Rectal resection/pCR group 100%
  
  \[ P = 0.56 \]
When to take your decision? Before or after nCRT?

What is against wait and see?

- No definition of CCR
- You can’t be sure that LNs are free
- You can’t be sure that there is no residual tumors
- No correlation between clinical and pathological complete response
- You can only diagnose complete pathologic response after resection
- You don’t know if you are helping or harming your patient!! (No Randomized trials)

Julio Garcia 2011

The rationale of a "wait and see" policy relies on retrospective observations, which are currently insufficient to support this policy except in patients who are: Unfit for or Refuse radical surgery
When to take your decision? Before or after nCRT?

2- From APR to SP after Complete or Incomplete Clinical Response

Downsizing & Sphincter Preservation

- Tumor down-staging
  - Increases rate of sphincter preservation
  - German Rectal Cancer Trial & (NSABP) R-03 trial

When to take your decision? Before or after nCRT?

**Downsizing & Sphincter Preservation**

- Tumor down-staging
- No difference in sphincter preservation
- 2 Systematic Reviews

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**Why SP Surgery?**

- Not to lose the golden chance of cure if CCR
- T1 have 5% MLN
  - MLN % increases in T2 & T3
- No permanent Stoma
- Free CRM and DRM

Alexandria Main University Hospital
Health Insurance Hospitals
Between 1/2010 & 12/2014
Methods

- Prospective study: 45 pts (SP) 26 control (APR)
- Inclusion criteria:
  - T3
  - <1 cm distance between the top of the anal sphincter and the distal edge of the tumor
- Exclusion Criteria:
  - Mucinous carcinoma
  - Distant metastasis

When to take your decision? Before or after nCRT?

Methods

- Preoperative nCRT
- Final decision about sphincter preservation was intra-operative
- Surgery was done 8–12 weeks after completion of nCRT
- Criteria for changing operative strategy to SP:
  - Tumor downsizing that leaves ≥1 cm distal safety margin above the anal sphincters
  - Free potential CRM in MRI
When to take your decision? Before or after nCRT?

**Tumor Response**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
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</thead>
<tbody>
<tr>
<td>ycCR</td>
<td>12</td>
<td>27</td>
</tr>
<tr>
<td>TRG4 (ypCR)</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td>TRG3</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>TRG2</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>TRG1</td>
<td>10</td>
<td>22</td>
</tr>
</tbody>
</table>

**Study Group**

- 36 Pts TME & CAA
- 6 Pts ISRR (partial resection of IAS)
- 9 Pts TME & CRA
When to take your decision? Before or after nCRT?

**Oncologic outcome**

- Mean follow up 57 months
- CA specific 87.5%
- Overall survival 79%

<table>
<thead>
<tr>
<th></th>
<th>SP</th>
<th>APR</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Overall Recurrence</td>
<td>6/45</td>
<td>3/26</td>
<td>0.99</td>
</tr>
<tr>
<td>13.3%</td>
<td>11.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local Recurrence</td>
<td>4/45</td>
<td>1/26</td>
<td>0.64</td>
</tr>
<tr>
<td>8.8%</td>
<td>3.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean time for Recurrence (ms)</td>
<td>27.2</td>
<td>31.8</td>
<td>0.06</td>
</tr>
</tbody>
</table>
**Oncologic outcome**

**Salvage APR**

- 3/4 patients with local recurrence underwent salvage APR with free safety margins
- Follow-up after salvage surgery for 31, 33, and 37 months revealed no recurrences

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**Oncologic Outcome**

- Kaplan–Meier analysis (study group)
  - Disease-free Survival: 87%
  - Overall Survival: 88.9%
- Univariate analysis for factors affecting recurrence:
  - N2 stage
  - Low TRG
  - Pathologic response
Factors affecting recurrence

(a) ypN stage

Disease free survival

Numbers at risk

0 22 22 22 22 21 20 14
1 10 10 10 10 10 9 3
2 13 13 11 10 8 8 2

Log Rank test, p < 0.001

(b) Pathologic response

Disease free survival

Numbers at risk

CPR 10 10 10 10 9 8 6
RT 35 35 35 33 30 29 13

CPR= Complete pathologic response, RT= Residual tumor present.

P value (log rank test) = 0.43

When to take your decision? Before or after nCRT?
Factors affecting recurrence

When to take your decision? Before or after nCRT?

Conclusions

- Changing operative strategy from APR to SP after downstaging by nCRT:
  - T3 low rectal cancer
  - Favorable histopathology
  - Motivated patients
  - Good sphincter function
  - Strict follow-up
Conclusions

- Disease-free survival rates are comparable to patients having their decision made before nCRT
- Early diagnosis of recurrence and salvage surgery with free resection margins can be achieved

Thank You for Your Kind Attention