Colorectal Cancer: A Minimalist Approach
Sandy Hwang Fang, MD, FACS, FASCRS
Associate Professor
Disclosures

Consultant for Intuitive when I was at Johns Hopkins Hospital.
Objectives

1. Robotic surgery in colorectal cancer
2. Watch and Wait Approach to Rectal Cancer
Robotic total mesorectal excision
• Randomized clinical trial: robotic-assisted vs conventional laparoscopic surgery => open conversion rates
  – 29 sites, 10 countries, 40 surgeons
• 471 patients with rectal adenocarcinoma
  – Robotic assisted: 237 patients
  – Laparoscopic: 234 patients
• f/u: 30 days, 6 months
• No significant reduction in conversion to laparotomy
Effect of Robotic-Assisted vs Conventional Laparoscopic Surgery on Risk of Conversion to Open Laparotomy Among Patients Undergoing Resection for Rectal Cancer: The ROLARR Randomized Clinical Trial

David Jayne 1, Alessio Pigazzi 2, Helen Marshall 3, Julie Croft 3, Neil Corrigan 3, Joanne Copeland 3, Phil Quirke 4, Nick West 4, Tero Rautio 5, Niels Thomassen 6, Henry Tilney 7, Mark Gudgeon 7, Paolo Pietro Bianchi 8, Richard Edlin 9, Claire Hulme 10, Julia Brown 3

Table 3. Secondary End Points by Treatment Group

<table>
<thead>
<tr>
<th>End Point</th>
<th>No./Total No. (%)</th>
<th>Conventional Laparoscopic Surgery</th>
<th>Robotic-Assisted Laparoscopic Surgery</th>
<th>Unadjusted Risk Difference (95% CI), %</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRM+</td>
<td>14/224 (6.3)</td>
<td>12/235 (5.1)</td>
<td>1.2 (−3.1 to 5.4)</td>
<td>0.78 (0.35 to 1.76)</td>
<td>0.56</td>
</tr>
<tr>
<td>Mesorectal area = mesorectal plane</td>
<td>173/223 (77.6)</td>
<td>178/233 (76.4)</td>
<td>1.2 (−6.5 to 8.9)</td>
<td>0.94 (0.56 to 1.57)</td>
<td>0.14</td>
</tr>
<tr>
<td>Intraoperative complication</td>
<td>34/230 (14.8)</td>
<td>36/236 (15.3)</td>
<td>−0.5 (−6.0 to 7.0)</td>
<td>1.02 (0.60 to 1.74)</td>
<td>0.94</td>
</tr>
<tr>
<td>Postoperative complication within 30 d of operation</td>
<td>73/230 (31.7)</td>
<td>78/236 (33.1)</td>
<td>−1.3 (−9.8 to 7.2)</td>
<td>1.04 (0.69 to 1.58)</td>
<td>0.84</td>
</tr>
<tr>
<td>Postoperative complication &gt;30 d and ≤6 mo after operation</td>
<td>38/230 (16.5)</td>
<td>34/236 (14.4)</td>
<td>2.1 (−4.5 to 8.7)</td>
<td>0.72 (0.41 to 1.26)</td>
<td>0.25</td>
</tr>
<tr>
<td>Mortality within 30 d of operation</td>
<td>2/230 (0.9)</td>
<td>2/236 (0.8)</td>
<td>0.02 (−1.7 to 1.7)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CRM+, circumferential resection margin positivity; NA, not applicable.

a Adjusted for sex, body mass index class, preoperative radiotherapy, intended procedure, and operating surgeon.

b Defined as tumor cells within 1 mm of the circumferential resection margin on histological analysis.

c Adjusted analysis was not performed for mortality within 30 days of operation due to the small number of events.
• Randomized 1:1: robotic vs laparoscopic
  – South Korea, 3 surgeons
• Primary outcome: quality of TME
• 139 patients
  – Robotic: 66
  – Laparoscopic: 73
### Robot-assisted Versus Laparoscopic Surgery for Rectal Cancer: A Phase II Open Label Prospective Randomized Controlled Trial

Min Jung Kim, Sung Chan Park, Ji Won Park, Hee Jin Chang, Dae Yong Kim, Byung-Ho Nam, Dae Kyung Sohn, Jae Hwan Oh

**RG (n = 66)** | **LG (n = 73)** | **P**
---|---|---
Tumor size, cm, median (range) | 2.5 (0–6.0) | 2.1 (0–11.0) | 0.84
Number of harvested lymph nodes | Median 18.0 | 15.0 | 0.04
| Range 7.0–59.0 | 4.0–40.0 | 0.009
| <12, n (%) 6 (9.1) | 19 (26.0) | 0.009
| ≥12, n (%) 60 (90.9) | 54 (74.0) | 0.422
Tumor differentiation, n (%) | Well differentiated 9 (13.6) | 8 (11.0) | 0.99
| Moderately differentiated 53 (80.3) | 64 (86.2) | 0.32
| Poorly differentiated 3 (4.6) | 1 (1.4) | 0.14
| Mucinous 1 (1.5) | 0 (1.4) | 0.23
Tumor Regression Grade Scale, n (%) | 1 11 (16.7) | 11 (15.1) | 0.99
| 2 28 (42.4) | 31 (42.5) | 0.62
| 3 8 (12.1) | 10 (13.7) | 0.23
| 4 5 (7.6) | 6 (8.2) | 0.956
\(\text{p}\)ypT classification, n (%) | T0 5 (7.6) | 6 (8.2) | 0.956
| T1 2 (3.0) | 4 (5.5) | 0.53
| T2 8 (12.1) | 7 (9.6) | 1.0
| T3 17 (25.8) | 18 (24.6) | 0.62
| T4a 30 (45.5) | 36 (49.3) | 0.19
| T4b 2 (3.0) | 1 (1.4) | 0.009
\(\text{p}\)ypN classification, n (%) | N0 46 (69.7) | 56 (76.7) | 0.713
| N1a 9 (13.7) | 5 (6.9) | 0.11
| N1b 7 (10.6) | 6 (8.2) | 0.77
| N1c 2 (3.0) | 2 (2.7) | 0.62
| N2a 2 (3.0) | 3 (4.1) | 0.49
| N2b 0 (0) | 1 (1.4) | 0.23
Proximal resection margin, cm, median (range) | 12.3 (4.7–35.8) | 13.2 (6.8–29.0) | 0.727
Distal resection margin, cm, median (range) | 1.5 (0.04–6.7) | 0.7 (0–2.5) | 0.11
Radial resection margin, cm, median (range) | 0.7 (0–2.5) | 0.7 (0–1.8) | 0.53
Circumferential resection margin, n (%) | Positive (≤1 mm) 4 (6.1) | 4 (5.5) | 0.35
| Negative (>1 mm) 61 (92.4) | 68 (93.2) | 0.099
Quality of TME as rated by pathologist, n (%) | Complete 53 (80.3) | 57 (78.1) | 0.599
| Nearly complete 12 (18.2) | 16 (21.9) | 0.02
| Incomplete 1 (1.5) | 0 (0) | 1.0

*Data from patients with preoperative CRT or chemotherapy.
†One patient in each group had a peritonealized tumor.
CRT indicates chemoradiotherapy; TME, total mesorectal excision.
### Robot-assisted Versus Laparoscopic Surgery for Rectal Cancer: A Phase II Open Label Prospective Randomized Controlled Trial

**Kim, Min Jung; Park, Sung Chan; Park, Ji Won; Chang, Hee Jin; Kim, Dae Yong; Nam, Byung-Ho; Sohn, Dae Kyung; Oh, Jae Hwan**


doi: 10.1097/SLA.0000000000002321

#### Table 1: Postoperative Pathologic Outcomes

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<thead>
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<td>Tumor differentiation, n (%)</td>
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<td>Tumor Regression Grade Scale, n (%)</td>
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<td>pT classification, n (%)</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>T1</td>
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<td>0.531</td>
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<tr>
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<td></td>
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<td>0.599</td>
</tr>
<tr>
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<td>16 (21.9)</td>
<td></td>
</tr>
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<td>0 (0)</td>
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*Data from patients with preoperative CRT or chemotherapy.
†One patient in each group had a peri tonealized tumor.
CRT indicates chemoradiotherapy; TME, total mesorectal excision.
Watch and Wait: Rectal Cancer Organ Preservation
**Rectal Cancer**

### CLINICAL STAGE

T3, N any with involved or threatened CRM (by MRI)\(^n\);
T4, N any or Locally unresectable or medically inoperable

### TOTAL NEOADJUVANT THERAPY

- Long-course chemo/RT\(^q, r\)
  - Capcitabine\(^P\) or infusional 5-FU\(^P\)
  - or Short-course RT\(^r, u\)

### PRIMARY TREATMENT

- Transabdominal resection\(^l, v, x\)
  - Surveillance (REC-11)
  - Restaging\(^c\)
  - Resection contraindicated

- Chemotherapy (12–16 wk)
  - FOLFOX or CAPEOX
  - Consider FOLFIRINOX (for T4, N+)

- Long-course chemo/RT\(^q, r\)
  - Capcitabine\(^P\) or infusional 5-FU\(^P\)
  - or Short-course RT\(^r, u\)

- Systemic therapy\(^w\)

### RESTAGING

- Restaging\(^c\)
  - Resection contraindicated

- Surveillance (REC-11)
  - Systemic therapy\(^w\)

**Note:**

- \(^l\) Loco-regional
- \(^v\) Celiac nerve plexus
- \(^x\) Inferior vena cava
- \(^n\) Necrosis
- \(^P\) Peri-lesional
- \(^r\) Rectal
- \(^u\) Ulcer
- \(^c\) Clinical
<table>
<thead>
<tr>
<th></th>
<th>Complete Response</th>
<th>Near Complete Response</th>
<th>Incomplete Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopy</td>
<td>Flat, white scar</td>
<td>Irregular mucosa</td>
<td>Visible tumor</td>
</tr>
<tr>
<td></td>
<td>Telangiectasia</td>
<td>Small mucosal nodules or minor mucosal abnormality</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No ulcer</td>
<td>Superficial ulceration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No nodularity</td>
<td>Mild persisting erythema of the scar</td>
<td></td>
</tr>
<tr>
<td>Digital Rectal Exam</td>
<td>Normal</td>
<td>Smooth induration or minor mucosal abnormalities</td>
<td>Palpable tumor nodules</td>
</tr>
<tr>
<td>MRI-T2W</td>
<td>Only dark T2 signal, no intermediate T2 signal</td>
<td>Mostly dark T2 signal, some remaining intermediate signal</td>
<td>More intermediate than dark T2 signal, no T2 scar</td>
</tr>
<tr>
<td></td>
<td>AND</td>
<td>AND/OR</td>
<td>AND/OR</td>
</tr>
<tr>
<td></td>
<td>No visible lymph nodes</td>
<td>Partial regression of lymph nodes</td>
<td>No regression of lymph nodes</td>
</tr>
<tr>
<td>MRI-DW</td>
<td>No visible tumor on B800-B1000 signal</td>
<td>Significant regression of signal on B800-B1000</td>
<td>Insignificant regression of signal on B800-B1000</td>
</tr>
<tr>
<td></td>
<td>AND/OR</td>
<td>AND/OR</td>
<td>AND/OR</td>
</tr>
<tr>
<td></td>
<td>Lack of or low signal on ADC map</td>
<td>Minimal or low residual signal on ADC map</td>
<td>Obvious low signal on ADC map</td>
</tr>
<tr>
<td></td>
<td>Uniform, linear signal in wall above tumor is ok</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Clinical Incomplete Response
Clinical Complete Response
• Treatment
  – 25 Gy in 5 fractions
  – FOLFOX x 8 cycles or CAPOX x 5 cycles
• June 2016-March 2019: 19 patients
• Treatment with SCRT and chemotherapy resulted in high cCR rate, intact anorectal function, and no severe late effects
Surveillance Protocol: NCCN
(In addition to CT C/A/P, CEA, colonoscopy)

• DRE

• Proctoscopy
  – Every 3-4 months x 2 years
  – Then every 6 months for a total of 5 years

• Rectal cancer protocol MRI
  – Every 6 months for at least 3 years to monitor for extraluminal local recurrence
  – Then annually for a total of 5 years (OHSU)
ReSARCh (Rectal Sparing Approach after preroperative Radio-and/or Chemotherapy) Trial

Rectal Sparing Approach After Neoadjuvant Therapy in Patients With Rectal Cancer: The Preliminary Results of the ReSARCh Trial

- **Prospective Observational Trial**
  - NCT02710812

- **17 Italian Hospitals**
- **160 patients**
  - Male 104, Female 56

- Rectal cancer after neoadjuvant therapy, fit for TME surgery

- **12-Weeks Restaging**
  - *≈* 64 Major Clinical Response
  - 96 Complete Clinical Response

- **24-Months Median Follow-Up**
  - 98 Local Excision
  - 3 Clavien-Dindo ≥ 3
  - 26 completion TME required
  - 11 completion TME performed
  - 10 no residual cancer at histopathology

- **62 Watch-and-Wait**

Marchegiani et al., Ann Surg Oncol.
Visual Abstract by @GayaSpolverato for @AnnSurgOncol

ANNALS OF SURGICAL ONCOLOGY
Organ Preservation in Rectal Adenocarcinoma (OPRA): ongoing

- Objective: Phase II randomized controlled trial, multi-institutional: total neoadjuvant therapy and selective non-operative management in locally advanced rectal cancer
**Fig. 1** Trial schema. MSKCC-based multi-institutional, Phase II trial schema underway to test the feasibility of incorporating a NOM approach to the multimodality treatment of rectal cancer. This study will evaluate the 3-year DFS in LARC patients treated with CRT plus induction or consolidation chemotherapy and TME or NOM (https://clinicaltrials.gov/ct2/show/NCT02008656?term=NCT02008656&rank=1)

*Patients with tumor progression at the interval evaluation will be treated according to standard of care.*
Thank you! Questions??