SURGICAL MANAGEMENT OF COLORECTAL CANCER

Irinel Popescu, MD, FACS, FEBS
Professor of Surgery

Dan Setlacec Center of General Surgery and Liver Transplantation
Fundeni Clinical Institute, Bucharest
Colorectal cancer – multimodal treatment

- Interventional endoscopy
- Surgery
- Chemotherapy
- Radiotherapy
- Interventional radiology
Colorectal carcinoma—TNM staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIB</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIC</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>IIIA</td>
<td>T1-2</td>
<td>N1/N1c</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td>IIIB</td>
<td>T3-T4a</td>
<td>N1/N1c</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2-T3</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1-T2</td>
<td>N2b</td>
<td>M0</td>
</tr>
<tr>
<td>IIIC</td>
<td>T4a</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3-T4a</td>
<td>N2b</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4b</td>
<td>N1-N2</td>
<td>M0</td>
</tr>
<tr>
<td>IVA</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
</tr>
<tr>
<td>IVB</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
</tr>
</tbody>
</table>
I. COLON CANCER
A. Carcinoma in a polip
Non-invasive carcinoma (Tis)

- Endoscopic removal (polypectomy)
  - effective treatment as long as the resection margins are free of cancer

Negative resection margin
B. Localized invasive colon cancer (T1-4, N0-2, M0)
T1 carcinoma (in a polyp)

- Endoscopic resection
  - Reasonable alternative to radical surgery
    - Favorable risk, T1 colon cancers arising in a polyp

- Higher risk of residual cancer or nodal metastases:
  - Poorly-differentiated histology
  - Lymphovascular invasion
  - Cancer at the resection or stalk margin
  - Invasion into the muscularis propria (T2)
  - Sessile polyp with lower third submucosal penetration

Tattoo the area of endoscopic resection
Radical surgery

- The only curative treatment modality for localized invasive colon cancer (T1-4, N0-2, M0)

- Goals of surgery:
  1. Complete removal of:
     1. the tumor
     2. the major vascular pedicle(s)
     3. the lymphatic drainage basin of the affected colonic segment
  2. Restoration of bowel continuity
1. Complete resection
The concept of “Complete Mesocolic Excision with Central Vascular Ligation” – Hohenberger

Complete mesocolic excision (CME) – “en bloc” removal of

- the tumor bearing colon
- its associated lympho-vascular supply
- ligation of the mesocolic vessels near their origin

By taking the colon and mesocolon in an intact “envelope “of visceral peritoneum
CME – Three essential components

1. Dissection between mesenteric plane and parietal fascia

2. Central vascular tie
   1. Complete removal of LN towards central direction (A, B)

3. Adequate length of bowel
   1. Complete removal of pericolic LN – longitudinal direction (C)

- Adequate lymphadenectomy

- Mesocolic plane
- Intramesocolic plane
- Muscularis propria plane
CME – Mesocolic plane

- CME allows for higher quality of surgical specimens when compared to less radical “standard” surgery.
- Dissection plane significantly impacts loco-regional control and thus overall survival.

P value < 0.05
CME – Central vascular ligation

- CORECT vascular ligation for cancer
- INADEQUATE vascular ligation for cancer
Why Central Vascular Ligation?

- Allows for a complete lymphadenectomy
  - LN along the mesocolic border of the colon (epicolic, pericolic)
  - the regional mesenteric lymph nodes along:
    - the vascular arcades (intermediary)
    - the origin of the major mesenteric vessels (principal)
CME – Complete lymphadenectomy

- The higher the number of LN harvested
- The better staging
  - Stage migration (stage II → stage III)

Table 2. Lymph Node Retrieval Data for Patients From Erlangen and Leeds

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Erlangen</th>
<th>Leeds</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median No. of lymph nodes retrieved</td>
<td>30</td>
<td>18</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>IQR</td>
<td>23-39</td>
<td>12-24</td>
<td></td>
</tr>
<tr>
<td>Positive nodes retrieved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients</td>
<td></td>
<td></td>
<td>.241</td>
</tr>
<tr>
<td>Median</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>0-2</td>
<td>0-3</td>
<td></td>
</tr>
<tr>
<td>N1/2 patients</td>
<td></td>
<td></td>
<td>.923</td>
</tr>
<tr>
<td>Median</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>1-6</td>
<td>1-6</td>
<td></td>
</tr>
<tr>
<td>Negative nodes retrieved</td>
<td></td>
<td></td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>All patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>28</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>21-38</td>
<td>10-22</td>
<td></td>
</tr>
<tr>
<td>N1/2 patients</td>
<td></td>
<td></td>
<td>&lt; .0001</td>
</tr>
<tr>
<td>Median</td>
<td>26</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>IQR</td>
<td>18-33</td>
<td>5-17</td>
<td></td>
</tr>
</tbody>
</table>
CME — Better staging

- Stage I (T2, N0, M0): NO adjuvant chemotherapy
- Stage II (T3/T4, N0, M0): Chemotherapy – high-risk patients
- Stage III (any T, N1/N2, M0): Chemotherapy – all patients

Inadequate surgical resection/pathologic evaluation

Inadequate adjuvant chemotherapy allocation

Better staging allows a more correct adjuvant treatment
The number of LN evaluated was positively associated with survival

The number of LN evaluated – measure of the quality of CRC care

<table>
<thead>
<tr>
<th>Source, y (reference)</th>
<th>No. of patients</th>
<th>No. of lymph nodes</th>
<th>Overall survival, %</th>
<th>HR or RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCDB, 2003 (8)</td>
<td>35787</td>
<td>1–7</td>
<td>49.8</td>
<td>1.0 (referent)†</td>
<td>&lt;.001‡</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8–12</td>
<td>56.2</td>
<td>0.81 (0.77 to 0.84)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥13</td>
<td>63.4</td>
<td>0.68 (0.65 to 0.71)</td>
<td></td>
</tr>
<tr>
<td>Kentucky Cancer Registry, 2004 (17)</td>
<td>2437</td>
<td>1–12</td>
<td>56</td>
<td>–</td>
<td>&lt;.001‡</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;12</td>
<td>63</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Uppala/Orebro Registry, 2005 (19)</td>
<td>3735</td>
<td>1–11</td>
<td>~65</td>
<td>–</td>
<td>&lt;.001‡</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;11</td>
<td>~75</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Ontario Registry, 2006 (16)</td>
<td>1000</td>
<td>1–3</td>
<td>–</td>
<td>1.0 (referent)§</td>
<td>.59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4–6</td>
<td>–</td>
<td>0.9 (0.6 to 1.3)</td>
<td>.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7–9</td>
<td>–</td>
<td>0.9 (0.6 to 1.3)</td>
<td>.53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10–36</td>
<td>–</td>
<td>0.6 (0.4 to 1.0)</td>
<td>.03</td>
</tr>
<tr>
<td>SEER registry, 2002 (18)</td>
<td>8574</td>
<td>Each additional lymph node</td>
<td>–</td>
<td>0.98 (0.97 to 0.98)</td>
<td></td>
</tr>
</tbody>
</table>
Rationale for CME

- The “envelope” of visceral peritoneum contains potentially metastatic lymph nodes (LN).
- By keeping intact the “envelope” minimize the risk of spillage of cancer cells into the peritoneal cavity.
- Central vascular ligation of the relevant blood supply improves the number of lymph nodes (LN) harvested.

Decreases the 5 year local recurrence rate
Increases the 5 year cancer related survival
Colon cancer: CME – standard of care

- Complete mesocolic excision with central vascular ligation should become the standard approach to colon carcinoma
- These approach (CME) decreases the local recurrence rates and increases overall survival in stage I-III colon cancer patients
Types of colon resections

- Right colectomy
- Extended right colectomy
Types of colon resections

- Transverse colectomy
- Sub-total colectomy
Types of colon resections

- Left colectomy
- Total colectomy
Type of approach open vs laparoscopic

- Laparoscopic CME is feasible
- Short-term and long-term outcomes following laparoscopic CME were similar to those achieved by open approach in specialized centers.
Locally advanced colon cancer (T4)

- Invasion of contiguous organs or inflammatory adhesions involving neighboring structures – 10%

Treatment objectives:
- “En-bloc” multivisceral resection with a negative margin of the adjacent structure
- The plane of adherence between the colonic tumor and the adjacent organ(s) should not be disrupted
  - 40% of these adhesions are malignant
  - Transection of tumor could further impair prognosis.
2. Restoration bowel continuity
Uncomplicated tumors

- Primary anastomosis
  - Ileo-colicostomy
  - Colo-colicostomy
  - Colo-rectostomy
Colonic obstruction

- resection of the tumor with a primary anastomosis
  - with or without a temporary proximal diversion

- resection without anastomosis – end colostomy

- proximal diversion with a mucous fistula or a loop colostomy, followed by elective definitive resection (second operation)
Colonic perforation

- Resection of the tumor with a primary anastomosis
  - localized fluid collection/abscess

- Resection without anastomosis – end colostomy
  - free perforation
  - diffuse peritonitis
  - patient is medically unstable
II. RECTAL CANCER
Non-invasive carcinoma (Tis)

- Endoscopic removal (polypectomy)
  - effective treatment as long as the resection margins are free of cancer

- Transanal excision (TAE) – lesions located in the anal canal (less than 4 cm from anal verge)
Localized invasive rectal cancer (T1–4, N0–2, M0)

SURGICAL RESECTION
A. Local excision procedures
Techniques

- Transanal excision (TAE)
  - ADK below 4 cm from anal verge

- Transanal endoscopic microsurgery (TEM)
  - ADK 4-15 cm from anal verge

Goal:
- full-thickness excision of the rectal cancer
- minimum lateral margin of 1 cm
- histologically negative deep margin
- primary closure
Indications TAE/TEM

- **Standard:**
  - T1 cancers < 3 cm
  - No radiographic evidence of positive regional LN (N0)
  - Low risk pathologic features
    - well differentiated
    - no vascular or neural invasion
  - Compliance with aggressive postoperative surveillance
Results TAE/TEM

- T1N0 patients – low risk factors:
  - Significantly fewer postoperative complications than following major resections
  - Local recurrence rates are comparable to more extensive operative procedures (4-6%)
  - 10-year OS – 98%
  - 10-year DFS – 92%
Higher risk patients (pathology)

- > T1
- > 3 cm
- Inadequate margins
- Lympho-vascular invasion

Immediate Reoperation (sphincter-saving/ APR)

Chemoradiotherapy (improves results)

Follow-up (aggressive)
Specific indications for TAE/TEM:

- Patients > T1 or >3 cm:
  - Complete response following chemoradiation
  - Refusal of major abdominal surgery
  - Comorbidities that preclude a major intra-abdominal operation
  - Distant disease (short life expectancy)

Higher recurrence rates than following major resections
Lower survival rates compared with major operations
Response to chemoradiation

- Complete clinical response
  - Normal CEA level
  - Digital rectal examination
  - CT/endorectal ultrasonography
  - Absence of any residual scar, mass or ulcer

Near-complete clinical response
- Suspicious, small residual lesions
- Full-thickness local excision

Negative pathological result

Positive pathological result
- Rectal resection

Watch and Wait (A. Habr-Gama)
Watch and Wait – results

- Aggressive follow-up – mandatory
- Local recurrence rate: 11-31%
  - Disease recurrence may occur at any time
- Salvage therapy – local excision/rectal resection
  - Salvage rate – 93%
- 5-yr local recurrence-free survival: 87%
- 5-yr cancer specific DFS – 68%
- 5-yr cancer-specific OS – 91%
Endoscopic/Local excision procedures — curative attempt?

- **Tis/T1 N0 colorectal carcinomas**
  - Endoscopic resections or local excision procedures could be curative
    - Lower morbidity rates
    - Similar local recurrence rates vs. Rectal resections
    - Similar survival rates

- “Watch and wait” could be an acceptable option in patients with complete clinical response after neoadjuvant chemoradiotherapy
B. Rectal resections
Indications: T2–4,N0–2,M0

- Objectives
  1. Removal
     1. Distal colon and tumor-bearing rectum
        1. at least 2 cm away from distal tumor edge
     2. Lymph nodes and relevant vessels (IMA&IMV)
     3. Mesorectum (total mesorectal excision – TME)
  2. Restoration of bowel continuity – whenever possible
     1. Sphincter-sparing procedures
The concept of mesorectum; mesorectal fascia – Thoma Ionnescu

- Mesorectum – lipoma-like “envelope” of the rectum

- Mesorectal fat – surrounded by mesorectal fascia

- Mesorectal fascia:
  - 1894 – Thoma Ionnescu – “Gaine fibro-sereuse du rectum”
  - 1899 - Wilhelm von Waldeyer – “Fascia propria recti”
Total Mesorectal Excision (TME) – Heald

- Mesorectum – it may contain carcinoma cells and metastatic LN
- TME – removes completely the tumor, regional spread cells and loco-regional LN

Decreases local recurrence rates
Heald’s “Holly-plane” surrounding mesorectum

- Sharp & meticulous dissection surrounding mesorectal fascia
  - Posterior – easy to find
  - Anterior – less obvious
  - Lateral – the most difficult

- Correct TME – Intact circumferential resection margins (CRM)
  - intact mesorectal fascia
Importance of CRM

- CRM – the most important pathologic variable in patients undergoing TME
- Positive CRM – independent predictor of:
  - local recurrence
  - inferior survival

If pretreatment evaluation reveals tumor within 2 mm of the mesorectal fascia

Neoadjuvant chemoradiotherapy

T3/T4
N1/N2
TME – longitudinal extension

- The distal mesorectal excision margin – 5 cm below the lower border of the tumor
TME – Clinical relevance

- Total mesorectal excision significantly improved local recurrence and survival rates in rectal cancer patients
Tumor location – type of resection

- Low stapled (High anal)
- Manual transanal (Low anal)
- Amputation (APR)
1. Sphincter-sparing procedures
Indications

- Invasive rectal cancers beyond the submucosa
  - T2-4,N0-2,M0

- Histologically proven negative distal margin – R0

- Predicted adequate posttreatment anorectal sphincter function
Anterior Resection – AR

- **Indications**
  - Cancers located in the upper third of the rectum
    - 11-15 cm

- **Surgical technique**
  - Removal of the sigmoid colon and rectum to a level where the distal margin is free of cancer
  - Primary anastomosis between the descending colon and the middle rectum
Low Anterior Resection — LAR

- **Indications**
  - Cancers located to middle third of the rectum
    - 6-11 cm.

- **Surgical technique**
  - Removal of the sigmoid colon and rectum to a level where the distal margin is free of cancer
  - Primary anastomosis between the descending colon and distal rectum
Ultra-low anterior resection with “low-stapled” anastomosis

- **Indications**
  - distal rectal cancer – above the anal sphincter (5-6 cm.)

- **Surgical technique**
  - The rectum – transected just above the pelvic floor musculature
  - Anastomosis: colon – low rectum
    - Straight C-R anastomosis
    - Colonic J-pouch reservoir
    - Transverse coloplasty
Ultra-low anterior resection with transanal mucosectomy

- **Indications**
  - distal rectal cancer that does not invade the anal sphincter (4-5 cm.)

- **Surgical technique**
  - Muscularis propria of the rectum – transected at pelvic floor musculature
  - Transanal mucosectomy
  - Anastomosis: colon - anal sphincter
    - Straight colo-anal
    - Colonic J-pouch reservoir
    - Transverse coloplasty
ULER with intersphincteric dissection + coloanal anastomosis

- **Surgical technique**
  - At the pelvic floor musculature the dissection continues between internal and external anal sphincters
  - Perineal intersphincteric dissection
  - Anastomosis: colon – anal sphincter
Sphincter-sparing procedures

- By improving surgical expertise, the number and the types of sphincter-saving procedures increased continuously in the last decade
2. Abdominal-perineal resection
Indications

- Low-lying rectal adenocarcinomas
  - Negative distal margin of resection cannot be achieved with sphincter-sparing procedures
- Salvage procedure for local recurrence or locally advanced rectal cancer
- It remains the standard against which sphincter-sparing procedures and local excision procedures are compared
Surgical technique

- Resection of the
  - Sigmoid colon
  - Rectum
  - Anus

- Construction of a permanent colostomy
Drawbacks – APR

- Absence of mesorectal margin “cushion”
- Difficult technical dissection due to lack of planes
  - ‘Waist” of the specimen
- High rates of CRM involvement
- Perforation of the bowel
- Higher rates of local recurrence
- Lower rates of survival
Levator muscles are excised “en-bloc” with mesorectum, lower rectum and anus

Avoids “waist” of the specimen (APR)
ELAPE - Advantages

- Reduces bowel perforation
- Reduces circumferential resection margins (CRM) positivity
- Lower local recurrence rates

---

**Leeds + 11 European centres: Conventional vs Extralevator APR**

<table>
<thead>
<tr>
<th>Case series</th>
<th>Conventional</th>
<th>Extralevator</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>N = 124</td>
<td>N = 176</td>
</tr>
</tbody>
</table>

- Perforation: 28.2% vs 8.2%
  - P < 0.025
- CRM pos: 49.6% vs 20.3%
  - P < 0.0001

---

**Beijing RCT: Conventional vs Extralevator APR**

<table>
<thead>
<tr>
<th>RCT</th>
<th>Lithotomy</th>
<th>Prone</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008-2010</td>
<td>N = 32</td>
<td>N = 35</td>
</tr>
<tr>
<td>Perforation</td>
<td>5 (16%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>P &lt; 0.246</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRM pos</td>
<td>9 (28%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>P &lt; 0.013</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local recurrence (29 months)</td>
<td>6 (19%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>P &lt; 0.048</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

West, Br J Surg 2010; 97: 588
Han, Am J Surg 2012; 204: 274
Short-term and long-term outcomes following laparoscopic/robotic rectal resections were similar to those achieved by open approach
Locally advanced rectal cancer—T4

“En-bloc” multivisceral resections:
- Rectal cancer
- Adjacent organs invaded (R0)

Total pelvic exenteration (TPE)
- Rectum
- Bladder
- Internal reproductive organs
  - Prostate + seminal vesicles
  - Uterus, ovaries and vagina
Modified exenterations

- Posterior pelvic exenteration (PPE)
  - rectum, anus
  - uterus, ovaries
  - posterior vaginal wall

- Supralevator exenteration
  - TPE/PPE with a primary colo-rectal anastomosis

- Composite resections
  - Exenterative procedures including resection of bony structures
    - Sacrum
    - Coccyx
III. METASTATIC COLORECTAL CANCER
Initially resectable or initially unresectable: ESMO guidelines 2014

Patient Group 0
• Primarily technically R0-resectable liver or lung metastases
• No contraindications to resection

Patient Groups 1–3
• Initially unresectable mCRC, including:
  • Potentially resectable after CT (Group 1)
  • Disseminated disease, technically ‘never’/unlikely resectable (Group 2)
  • Never-resectable metastatic disease (Group 3)

Curative intent resection:
- Primary tumor and
- Liver/lung Metastases

Synchronous resectable CLMs (Group 0 - ESMO)

Curative-intent resection of primary tumor

<table>
<thead>
<tr>
<th>Delayed liver resection</th>
<th>Simultaneous resection</th>
<th>Liver-first approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications of the primary:</td>
<td>All the patients, except for:</td>
<td>- Borderline resectable SCLMs (difficult major hepatectomy)</td>
</tr>
<tr>
<td>- Perforation</td>
<td>- Complications of the primary</td>
<td>- T3-4/N1-2 rectal carcinoma (requiring radiotherapy)</td>
</tr>
<tr>
<td>- Obstruction</td>
<td>- Difficult major hepatectomy</td>
<td></td>
</tr>
<tr>
<td>- Bleeding</td>
<td>- Difficult rectal resection</td>
<td></td>
</tr>
</tbody>
</table>
Potentially resectable CLMs (Group 1 - ESMO)

Curative-intent resection of primary tumor

A
Hepatectomy following PVE/PVL or ALPPS
FLR < 30%

B
“Two-stage” hepatectomy
Few LM >30 mm in FLR

C
Hepatectomy + RFA
< 3 LM, < 30 mm in FLR

D
Hepatectomy following conversion CHT
Few bilobar CLMs
mCRC – Groups 0 and 1 (ESMO)

- The presence of potentially resectable liver/lung metastases should not be a contraindication for a curative-intent surgery in colorectal carcinoma.
Never resectable metastatic disease (Groups 2/3 – ESMO)

- Palliative surgery for complications of the primary
  - Perforation – palliative resection
  - Hemorrhage – palliative resection
  - Obstruction – palliative resection
    - internal diversion
    - colostomy