Management of Rectal Cancer

*Standardization of Care*
Financial Disclosure

- I have no financial disclosures.
Objectives

1. Assess the impact of rectal cancer on Kentucky.
2. Discuss the diagnosis and management of rectal cancer.
3. Outline the measures of quality in rectal cancer care.
FIGURE 1 Anatomy of the rectum.
<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-T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II A</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II B</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II C</td>
<td>T4b</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>III A</td>
<td>T1-T2</td>
<td>N1/N1c</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2a</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>N2a</td>
<td>N1-N2c</td>
<td>M0</td>
</tr>
<tr>
<td>IV A</td>
<td>Any T</td>
<td>Any N</td>
<td>M1a</td>
</tr>
<tr>
<td>IV B</td>
<td>Any T</td>
<td>Any N</td>
<td>M1b</td>
</tr>
</tbody>
</table>

**Primary Tumor (T)**
- **Tx**: Primary tumor cannot be assessed
- **T0**: No evidence of primary tumor
- **Tis**: Carcinoma in situ: intraepithelial or invasion of lamina propria
- **T1**: Tumor invades submucosa
- **T2**: Tumor invades muscularis propria
- **T3**: Tumor invades through the muscularis propria into pericoleal tissue
- **T4a**: Tumor penetrates to the surface of the visceral peritoneum
- **T4b**: Tumor directly invades or is adherent to other organs or structures

**Regional Lymph Nodes (N)**
- **Nx**: Regional lymph nodes cannot be assessed
- **N0**: No regional lymph node metastasis
- **N1**: Metastasis in 1-3 regional lymph nodes
- **N1A**: Metastasis in 1 regional lymph node
- **N1B**: Metastasis in 2-3 regional lymph nodes
- **N1C**: Tumor deposit(s) in the subserosa, mesentery, or nonperitonealized pericolic or perirectal tissues without regional nodal metastasis
- **N2**: Metastasis in 4 or more regional lymph nodes
- **N2A**: Metastasis in 4-6 regional lymph nodes
- **N2B**: Metastasis ≥7 regional lymph nodes

**Distant Metastasis (M)**
- **M0**: No distant metastasis
- **M1**: Distant metastasis
- **M1A**: Metastasis confined to 1 organ or site
- **M1B**: Metastases in >1 organ/site or the peritoneum
Improve care of the surgical patient
Safeguard standards of care
Education + Research
Advocacy and Health Care Policy
Civic and Military Collaboration and Partnership
Physician Support
Community Support
and.....

**Quality** Programs
1917: Issued minimum standards for hospitals; “Joint Commission”

1922: Commission on Cancer

1950: Committee on Trauma

1998: American College of Surgeons Oncology Group (ACOSOG)

2004: ACS NSQIP

2005: National Accreditation Program for Breast Cancers

... Children’s Surgery Verification + MBSAQIP + Coalition for Quality in Geriatric Surgery + Surgeon Specific Registry....
Significant variability in rectal cancer treatment and outcomes.

- Treatment Options
- Utilization of Adjuvant Therapy
- Surgical Technique
- Post-Op Mortality
- Local Recurrence
- Stoma Incidence
- 5Y Survival

Specialization AND training AND volume
common purpose improving the quality of rectal cancer care via standard care pathways of evidence based treatment....
1. Total Mesorectal Excision (TME)
2. Specific pathology assessment to measure quality of surgery
3. Specialist imaging techniques to identify high risk of local recurrence
4. Utilization of effective neo-adjuvant and adjuvant therapy
5. MDT approach to patient care

...expectation to reproduce European success
22 Proposed Standards

- Program Management (7)
- Clinical Services (13)
- Quality Improvement (2)

Quality Indicators

- APR Rate
- Anastomotic Leak Rate
- 30-Day Mortality
- Involved CRM
- Involved Distal Margin
- Reoperation Rate
- Mesorectal Grade
- LN Yield > 12 Rate
- Local Recurrence Rate
- 3-Year DFS Rate
Is Standardization of Rectal Cancer Care Important?....

National level.....
How Experienced is the Typical US Rectal Cancer Hospital?

- **70%** of hospitals treat < 20 patients/year
- **6%** hospitals treat > 50 patients/year

<table>
<thead>
<tr>
<th>Number of Rectal Cancer Patients</th>
<th>Hospital Percent Distribution</th>
<th>Number of Hospitals</th>
<th>Patient Percent Distribution</th>
<th>Number of Patients¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>14.2</td>
<td>189</td>
<td>2.2</td>
<td>524</td>
</tr>
<tr>
<td>5-9</td>
<td>22.6</td>
<td>300</td>
<td>8.7</td>
<td>2,105</td>
</tr>
<tr>
<td>10-19</td>
<td>33.0</td>
<td>438</td>
<td>25.5</td>
<td>6,144</td>
</tr>
<tr>
<td>20-29</td>
<td>13.3</td>
<td>177</td>
<td>17.5</td>
<td>4,206</td>
</tr>
<tr>
<td>30-39</td>
<td>6.3</td>
<td>84</td>
<td>11.8</td>
<td>2,842</td>
</tr>
<tr>
<td>40-49</td>
<td>4.1</td>
<td>55</td>
<td>10.0</td>
<td>2,416</td>
</tr>
<tr>
<td>&gt;=50</td>
<td>6.3</td>
<td>84</td>
<td>24.2</td>
<td>5,821</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100.0</strong></td>
<td><strong>1,327</strong></td>
<td><strong>100.0</strong></td>
<td><strong>24,058</strong></td>
</tr>
</tbody>
</table>

¹Data from the National Cancer Database.
The association of hospital volume with rectal cancer surgery outcomes

Table 2 Outcomes of rectal cancer surgery according to hospital volume

<table>
<thead>
<tr>
<th>Hospital volume</th>
<th>[75%]</th>
<th>[8%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
<td>Low</td>
<td>Medium</td>
</tr>
<tr>
<td>Average yearly case volume</td>
<td>1–5</td>
<td>6–10</td>
</tr>
<tr>
<td>Number of hospitals</td>
<td>232</td>
<td>65</td>
</tr>
<tr>
<td>Number of patients</td>
<td>2,364</td>
<td>2,686</td>
</tr>
<tr>
<td>Mortality, N (%)</td>
<td>50 (2.1)</td>
<td>29 (1.1)</td>
</tr>
<tr>
<td>Complications&lt;sup&gt;b&lt;/sup&gt;, N (%)</td>
<td>524 (22)</td>
<td>644 (24)</td>
</tr>
<tr>
<td>Sphincter preservation&lt;sup&gt;c&lt;/sup&gt;, N (%)</td>
<td>1197 (51)</td>
<td>1485 (55)</td>
</tr>
<tr>
<td>Length of stay, (days, mean (SD))</td>
<td>9.7 (7.3)</td>
<td>9.2 (8.1)</td>
</tr>
</tbody>
</table>

Multivariate analysis of hospital volume:

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95 % CI)</td>
<td>p value</td>
</tr>
<tr>
<td>Hospital volume</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Middle</td>
<td>0.51 (0.32–0.80)</td>
<td>0.003</td>
</tr>
<tr>
<td>High</td>
<td>0.42 (0.24–0.71)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>≥65</td>
<td>5.06 (2.73–9.32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Male</td>
<td>1.89 (1.16–3.06)</td>
<td>0.009</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Non-White</td>
<td>0.73 (0.37–1.39)</td>
<td>0.319</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>2.21 (0.81–6.08)</td>
<td>0.114</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAR</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>APR</td>
<td>1.59 (1.06–2.37)</td>
<td>0.023</td>
</tr>
</tbody>
</table>
- Meta-analysis; 47 studies + 1,000,000 patients + 9000 hospitals + 9000 surgeons
- Volume-outcome relationship favors high-volume facilities and high-volume surgeons
- Reduced overall and in-hospital and intra-operative mortality
Changes in Treatment Patterns for Patients With Locally Advanced Rectal Cancer in the United States Over the Past Decade: An Analysis From the National Cancer Data Base

Helmneh M. Sineshaw, MD, MPH; Ahmedin Jemal, DVM, PhD; Chang...
Increased Utilization NACRT + Decreased Utilization of Adjuvant CRT + Decreased Surgery Alone

GOOD THING? ...... Still, What About the Other 40%? Variable Penetrance?

- Low- and Medium volume facilities are less likely to offer patients standard treatment:
  - African American or Hispanic
  - Lack of private insurance
  - Residence in a neighborhood with lower educational background

- Low- and Medium volume facilities have significantly lower 5Y DFS.
  - Is my neighborhood a worse prognostic indicator than tumor grade or LN (+)????
Important?.....

State level.....
"You don't need a colonoscopy, but I'm sending you for one because, quite frankly, I don't like you."

...via collaborative efforts
Colorectal Cancer Burden
In Kentucky 2017....

- 2,250 Diagnosed with Colon and Rectal Cancer Of Which....550+ Rectal Cancers
Colon and Rectal Cancer Incidence
Rank #1
U.S. 39.8/KY 50.0

Colon and Rectal Cancer Death
Rank #5
U.S. 14.8/KY 17.2
County-by-county.....Incidence and Mortality can reach $2+x$ US
Colorectal Cancer Rates Are Surging In Younger Patients

By Marie Rosenthal

Philadelphia—A growing number of younger patients are being diagnosed with aggressive colorectal cancer, even as the incidence of the disease among older patients has been decreasing. The incidence of colorectal cancer is expected to increase among patients under 50 years of age, with cases rising 3.1% annually while younger patients with colorectal cancer are experiencing increases of 1.5% annually.

According to the National Cancer Institute, colorectal cancer is the second leading cause of cancer deaths in the United States. The incidence of colorectal cancer among younger patients is rising due to factors such as increased prevalence of obesity, physical inactivity, and unhealthy diets.

“Screening colonoscopies and removing polyps starting at a younger age would undoubtedly be helpful if we set aside cost,” Dr. Zheng said. “Our study shows CRC diagnosed between 40 and 50 years of age accounts for more than 50% of young-onset CRC.”
If you were born in 1890, your risk of colorectal cancer would be...?
ARTICLE

Colorectal Cancer Incidence Patterns in the United States, 1974–2013

Rebecca L. Siegel, Stacey A. Fedewa, William F. Anderson, Kimberly D. Miller, Jiemin Ma, Philip S. Rosenberg, Ahmedin Jemal
...proportion of rectal cancer diagnosed in < 50Y increased from 14.5% to 29.2%
.....about the same as today....

colorectal cancer risk for “millennials” has escalated back to the level of those born in the late 1800s

b. 1990 has 4x risk of b.1950

?sporadic

?obesity
“Y-CRC” in Summary

- 3.2% annual percentage increase for rectal cancer in individuals less than 50Y
  - Median age 44
  - Mucinous or signet cell pathology
- Over next 10 years, 124% increase in rectal cancer incidence in 20-34Y
- 1 in 4 rectal cancers will be diagnosed in people younger than the traditional screening age
- Cause?.....
“Y-CRC” in Summary

1. JM  29M
2. EC  48F
3. TJ  42M
4. SH  44F
5. VC  34F
6. AL  18M
7. BA  22F
8. SB  50M
9. PB  42F
10. KG  39M
11. AS  26F
12. RO  50M

.....the most vulnerable patients are still being defined....
- Increasing incidence in < 50Y; 2nd in US
- Stable mortality in < 50Y; 17th in US
1\textsuperscript{st} in U.S. Lung and Bronchus
1\textsuperscript{st} Larynx
2\textsuperscript{nd} Kidney and Pelvis
3\textsuperscript{rd} Oral Cavity and Pharynx
3\textsuperscript{rd} Colon and Rectum
7\textsuperscript{th} Brain
7\textsuperscript{th} Non-Hodgkin's Lymphoma
8\textsuperscript{th} Melanoma
9\textsuperscript{th} Cervix

1\textsuperscript{st} Cancer All-Site Incidence
1\textsuperscript{st} Cancer All-Site Death
CRC is NO Longer a Single Pathologic Entity

- Normal Colon
  - APC
  - hMSH2
  - hMLH1 abnormalities (Hereditary Syndromes)
  - Methylation abnormalities

- Hyperproliferative epithelium
  - APC
  - hMSH2
  - hMLH1 inactivation

- Adenoma
  - K-ras mutation
  - DCC deletion
  - p53 deletion

- Carcinoma
  - Further accumulation of genetic abnormalities
High-Poverty Counties in the Appalachian Region

(Counties with Rates At Least 1.5 Times the U.S. Average)

County Economic Status and Distressed Areas in
Appalachian Kentucky, Fiscal Year 2015
High School Education vs Colorectal Cancer Screening Rate (2006-2010)

- High School Education vs Colorectal Cancer Screening Rate
- Linear (High School Education vs Colorectal Cancer Screening Rate)

$R^2 = 0.7989$
1st in Tobacco Use; 28%

Obesity 32%

No Physical Activity 30%
50th in U.S. Cancer Deaths
50th Preventable Hospitalizations
49th Smoking
49th High Cholesterol
48th Cardiac Heart Disease/Death
47th High Blood Pressure
47th Personal Income
46th Obesity
44th Air Pollution
41st Low Birth Weight
40th Children in Poverty
40th Stroke
38th Adult Diabetes
36th Occupation Fatalities
32nd High School Graduation
Colorectal Cancer Burden

All-Site Cancer Burden

Genetics

Health Literacy, Unhealthy Choices, and Poverty

Culture of Appalachia and Coal
Important?....

Local level..... our role as clinicians and surgical educators....
Speed or Velocity

Oxford comma
The “Trials”…

- Swedish Rectal Cancer Trial: RT improves OS + DFS + LR
- Dutch TME Trial: RT + TME > TME alone *(to reduce local recurrence)*
- German Rectal Cancer Trial: Pre-op RT > Post-op RT
- PROPSECT Trial: ?
The “Papers”....
Local Recurrence = 6% After TME
Cancer-Specific Survival = 70% @ 5Y After TME

Author Conclusion: 70-80% rectal cancer can be cured with TME alone
Complete TME

- High ligation of IMA + splenic flexure mobilization
- Complete sigmoid colon resection
- Identify left ureter (pelvic brim)
- Sharp dissection of presacral plane anterior to the endopelvic fascia and outside the mesorectal membrane
- Protect the fascia propria
- Identify and avoid hypogastric plexus/nerves
- Sharp dissection posterior to anterior to avoid “coning-in” and positive radial margin
- Identify and avoid sacral nerves at pelvic brim and pelvic floor (posterior and lateral); nervi erigentes
- Continue posterior dissection to pelvic; divide Waldyers fascia at inferior border of mesorectum
- Sharp dissection of lateral attachments towards anterior
- Anterior dissection includes intact Denonvilliers fascia and peritoneal reflection
- Divide rectum at appropriate level and maintain bi-lobed, intact appearance of mesorectum by protecting fascia propria

Not graded by pathologist
Higher leak rate with incomplete mob splenic flexure
Higher leak rate/stricture with using sigmoid colon as anastomosis
Role of circumferential margin involvement in the local recurrence of rectal cancer

I J Adam, M O Mohamdee, I G Martin, N Scott, P J Finan, D Johnston, M F Dixon, P Quirke

Figure 1: Cumulative frequency of local recurrence comparing presence or absence of tumour at circumferential resection margin (CRM) in patients who had potentially curative resection. (+) CRM = < 1mm

Local recurrence 80% v. 10%

Figure 4: Survival comparing presence or absence of tumour at the circumferential resection margin (CRM) in patients who underwent potentially curative resection.
(+) CRM equates to 12x risk for local recurrence
  - 9% v. 64%

(+) CRM is an independent determinant for survival (as is LN involvement)
  - 24% v. 74%

High frequency and wide variation in recurrence endorses “specialists”
MRI best selects patients for NACRT and best selects patients in which NACRT can be safely avoided with the same expectation of curative surgery

- All patients with rectal cancer should undergo pre-operative MRI
- Widest range of survival is demonstrated in patients with T3 tumors (most common; 80%)
- MR LN evaluation is most sensitive/specific with irregular border and mixed signal intensity (not size)
- MR can assess distance from tumor edge to potential CRM; predictive of local recurrence
- MR can assess EMVI, an important independent prognostic factor associated with local recurrence
Localised rectal cancer assessed by MRI

- T1-T3a-b<5mm
  - N0/N1
  - EMVI-
  - Tumour in mid/upper third of rectum
  - CRM clear
  - ‘Good’ risk
  - 5yr survival 85-90%
  - Primary surgery (TME)

- Locally advanced
  - T3>5mm or N2
  - Or EMVI+
  - CRM clear (>1mm)

- Potential CRM-positive disease
  - High risk of local recurrence +/- distant failure

- Low risk of local recurrence BUT high risk of distant failure, 50-60%

- Neoadjuvant capcitabine and oxaliplatin for 12 weeks then capcitabine 1650mg/m²/day continuously and radiotherapy for 6 weeks followed by TME 6 weeks after completion of chemoradiotherapy.

Proposed by Brown

Typical
Important?....
What is the CoC Proposing?....

- Develop of a Rectal Cancer Multi-Disciplinary Team (RC-MDT)
  - Defined members
  - Meet at least 2x/month
- Refine Clinical Services for Rectal Cancer Patients
  - Review pathology specimens to confirm diagnosis
  - Complete systemic and local tumor staging (CT/MRI) prior to tx
  - Standardize MRI reporting with critical elements
  - CEA
  - RC-MDT treatment plan discussed and summarized
  - Definitive treatment timing within 60 days of initial clinical visit
  - TME
  - Standardized operative and pathology reporting, including photo-document
  - RC-MDT outcomes discussed and summarized
  - Adjuvant therapy (50% of patients within 8 weeks of surgery)
- Quality Improvement
Inconsistent management and variable outcomes validates the need for standardized and centralized rectal cancer care in the US.

Quality improvement is ever more important in the setting of increased incidence of rectal cancer in the young population less than 50 years of age.

In addition to the significant benefits of NACRT and TME, the multi-disciplinary management of the rectal cancer patients will further improve clinical outcomes, survival, and research efforts.