Recent Advancements in Colorectal Carcinoma: Diagnosis & Treatment

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Global Burden & Changing Trends

Colorectal carcinoma refers to malignancies arising from the colon or rectum

CRC remains a leading cause of cancer mortality worldwide

Rising incidence of early-onset CRC (<50 years)

Shifting toward precision oncology and molecularly driven treatment

Risk Factors : Non-Modifiable Risk Factors

Age

- Risk increases markedly **after age 50**
- Rising incidence in **younger adults (30–50 years)**

Family History of CRC or Polyps

- First-degree relative with CRC significantly increases risk
- Higher risk if relative diagnosed **before age 50**

Genetic Syndromes

- **Lynch syndrome (HNPCC)** – accounts for 2–4% of CRC
- **Familial Adenomatous Polyposis (FAP)** – ~1% of CRC

[Other rare syndromes: MUTYH-associated polyposis, Peutz-Jeghers]

Risk Factors : Non-Modifiable Risk Factors

4. Personal History of Polyps or CRC

Adenomatous polyps (large, multiple, or dysplastic) increase risk

Previous CRC increases risk of new primary tumors

5. Inflammatory Bowel Disease

>Ulcerative colitis

>Crohn's disease Long-standing inflammation increases dysplasia

6. Prior Radiation to Abdomen/Pelvis

Especially childhood radiation or older prostate RT techniques

Modifiable Risk Factors (Lifestyle-Related)

1. Diet

- High intake of **red meat** and **processed meats**
- Low intake of **fruits, vegetables, whole grains**
- High-temperature cooking (grilling, frying) increases carcinogenic compounds

2. Physical Inactivity

- Sedentary lifestyle increases CRC risk

3. Obesity

- Stronger association in men
- Increases both incidence and mortality

Modifiable Risk Factors (Lifestyle-Related)

4. Type 2 Diabetes

- Independent risk factor even after adjusting for obesity

5. Smoking

- Long-term tobacco use increases CRC and polyp formation

6. Alcohol Consumption

- Moderate to heavy alcohol use increases risk

Emerging / Possible Risk Factors (From recent epidemiological trends)

- **Low Vitamin D levels**
- **Microbiome imbalance** (dysbiosis)
- **High sugar-sweetened beverage intake** (especially in early-onset CRC)
- **Environmental exposures** (under study)

Diagnosis :

History taking is the Key

1. Bowel-Related Symptoms

- Persistent **diarrhea or constipation**
- **Change in bowel habits** (frequency, consistency, timing)
- **Narrow / pencil-thin stools**
- Feeling of **incomplete evacuation** even after passing stool
- Urgency to defecate when there is no need

2. Bleeding-Related Symptoms

- Bleeding may be visible or occult
- **Rectal bleeding**
- **Blood in stool** (bright red or dark/tarry)
- Occult bleeding → **iron-deficiency anemia**

3. Abdominal Symptom

- Due to tumor growth, obstruction or inflammation
- **Abdominal pain**, cramping or discomfort
- **Gas, bloating**, or fullness
- Pain during bowel movements
- Discomfort when sitting (rectal tumors)

4. Systemic / Constitutional Symptoms

- **Unexplained weight loss**
- **Fatigue / weakness**
- **Low iron levels** (iron-deficiency anemia)
- Loss of appetite

5. Advanced / Metastatic Disease

- **Liver metastasis:** RUQ pain, jaundice, hepatomegaly
- **Lung metastasis:** cough, dyspnea
- **Peritoneal spread:** ascites, abdominal distension

Important Clinical Notes

- Early CRC may be **asymptomatic**
- **Family history of CRC** or polyps
- Symptoms often overlap with benign conditions (hemorrhoids, IBS, fissures)
- Persistent or unexplained symptoms warrant evaluation

Diagnosis

- History tells you what to look for
- Physical exam tells you where to look
- Investigations tell you what you already suspected

Diagnosis

- A complete history & Physical examination can be change Everything
- **Physical Examination**
- Abdominal exam
- Digital rectal examination (DRE)
- Assessment for pallor, cachexia, hepatomegaly

Diagnosis

- **Colonoscopy (Gold Standard)—**Complete colonoscopy with endoscopic Biopsy + pathology review
- **Histopathology**
- **Molecular & Genetic Testing (Now Standard of Care)**
- Imaging for Staging :

A. CT Scan (Chest + Abdomen + Pelvis)

B. MRI Pelvis (for Rectal Cancer)

  - T staging
  - Mesorectal fascia involvement
  - Nodal assessment
  - Planning neoadjuvant therapy

Diagnosis

C. Endorectal Ultrasound (ERUS)

- Useful for early rectal cancers (T1–T2)

D. PET-CT

- Not routine
- Used when:
  - CT findings equivocal
  - Suspected metastatic disease
  - Rising CEA with no detectable lesion

Diagnosis

E. Laboratory Tests :

- **CBC** → anemia (often microcytic)
- **LFTs** → elevated ALP may suggest liver metastasis
- **CEA (Carcinoembryonic Antigen)**
  - Not diagnostic
  - Useful for baseline and follow-up
  - **Stool-Based Screening Tests**
  - FIT (Fecal Immunochemical Test)
  - FIT-DNA
  - gFOBT (older test, declining use)

Histopathology

- **Biopsy confirms diagnosis**

Pathology report includes:

- Type (adenocarcinoma most common)
- Grade
- Depth of invasion (if polypectomy specimen)
- Lymphovascular invasion
- Perineural invasion

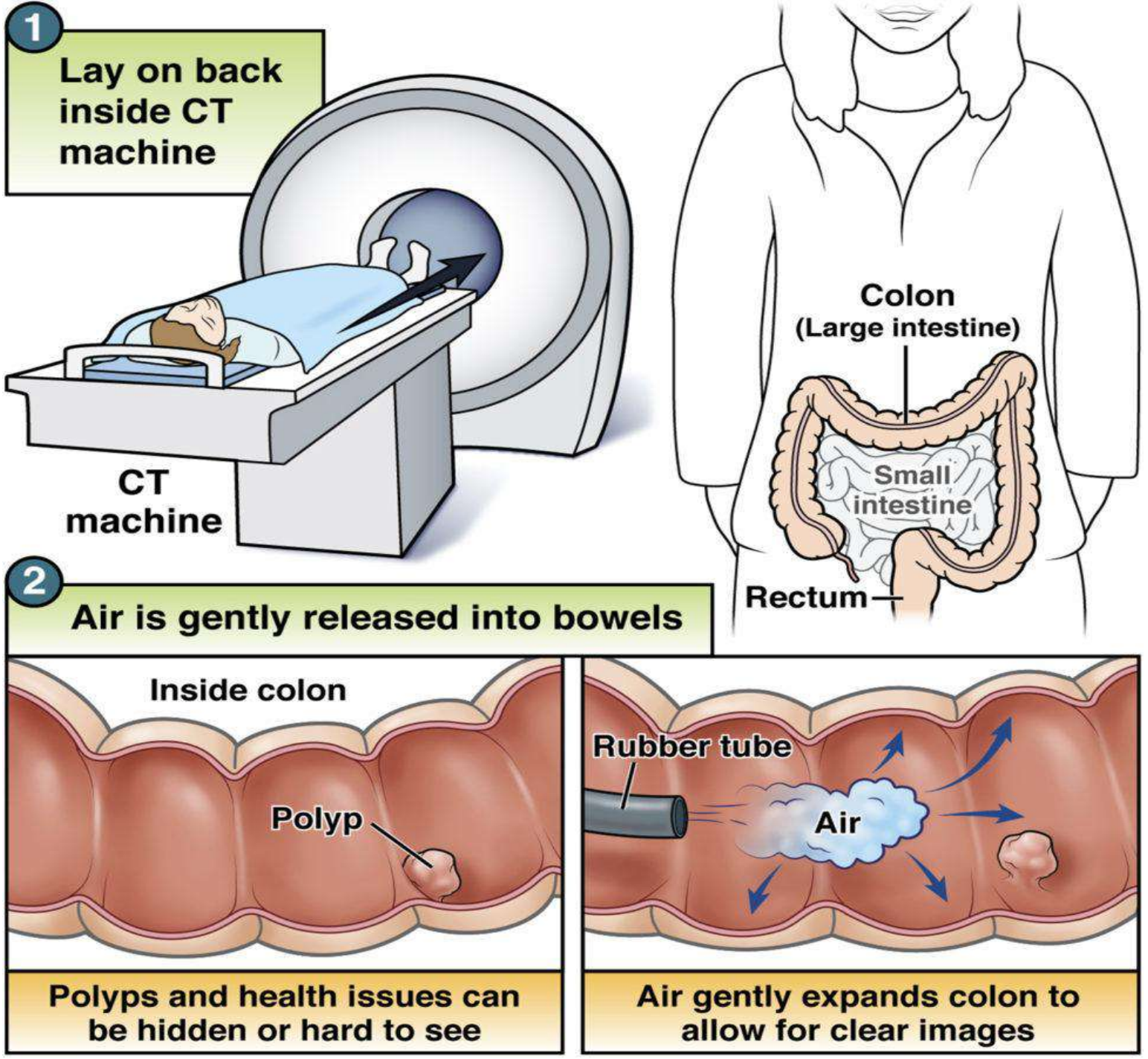
Advancement in Diagnosis

- CT colonography (If colonoscopy incomplete)
- Molecular & Genetic Testing (Now Standard of Care)
- AI-assisted Colonoscopy
- Liquid Biopsy

CT Colonography (Virtual Colonoscopy)

- Used when colonoscopy is incomplete or contraindicated
- Proximal lesion can be visualized in obstructed cases
- Increasingly used in Europe, USA, Japan

CT Colonography (Virtual Colonoscopy)



Molecular & Genetic Testing (Now Standard of Care)

1. IHC (Immunohistochemistry)

2. NGS (Next-Generation Sequencing)

Immunohistochemistry

IHC is a laboratory technique that uses antibodies to detect specific proteins in tumor tissue

IHC gives the biological behavior of the tumor — it tells us how the cancer is behaving

Immunohistochemistry is the first-line molecular screening tool

Immunohistochemistry

MMR proteins (MLH1, MSH2, MSH6, PMS2) → MSI status :

- Predicts immunotherapy response

- Screens for Lynch syndrome

- Identifies tumor differentiation patterns

- Guides prognosis

Molecular & Genetic Testing (Now Standard of Care)

Performed on biopsy or surgical specimen

Mandatory tests (per NCCN/ESMO 2025–2026):

1. **MMR/MSI** (for Lynch syndrome + immunotherapy eligibility)
2. **RAS mutation** (KRAS/NRAS)
3. **BRAF V600E**
4. **HER2 amplification**
5. **NTRK fusion** (rare but targetable)

NGS (Next-Generation Sequencing)

NGS is an advanced genetic test that sequences thousands of genes at once to identify mutations in the tumor DNA,RNA

Next-Generation Sequencing (NGS) is the comprehensive genomic mapping

NGS (Next-Generation Sequencing) in CRC

RAS mutations → anti-EGFR eligibility

BRAF V600E → prognosis + targeted therapy

HER2 amplification → HER2-targeted therapy

NTRK fusion → TRK inhibitors

Tumor mutational burden (TMB) → immunotherapy relevance

Liquid Biopsy — Emerging but Rapidly Growing

- Liquid biopsy is a non-invasive blood test that detects cancer-related genetic material circulating in the bloodstream without touching the tumor. It Detects :
    1. **ctDNA** (circulating tumor DNA) → most imp
    2. **CTCs** (circulating tumor cells)
    3. **cfRNA** (cell-free RNA)
    4. **Exosomes**

Liquid Biopsy (ctDNA) — Emerging but Rapidly Growing

- Detects **minimal residual disease (MRD)**
- Predicts recurrence than Imaging
- Used in USA, Europe, Australia, Japan
- Becoming standard in clinical trials
- Useful When Tissue Biopsy Is Difficult
- Costly
- **Not yet universal, but rapidly expanding worldwide.**

AI in Diagnosis :

- AI improves colonoscopy accuracy
- Reduces missed lesions
- Helps in:
  - Radiology imaging
  - Digital pathology
- Can detect patterns beyond human capability

Treatment Overview

- Treatment depends on stage and molecular profile
- Multidisciplinary approach is essential
- Includes:
  - Surgery
  - Chemotherapy
  - Radiotherapy
  - Targeted therapy
- Immunotherapy

Indications of Neoadjuvant Rx Rectal Carcinoma

A. Locally Advanced Rectal Cancer (LARC)

- T3 or T4 tumors
- Node-positive disease (N+)
- Threatened or involved mesorectal fascia (MRF)
- Low rectal tumors requiring sphincter preservation
- Tumors with high risk of local recurrence

B. To Improve Local Control

- Short-course radiotherapy (SCRT)
- Long-course chemoradiotherapy (LCCRT) Both improve **local control**, though not systemic control

Indications of Neoadjuvant Rx Rectal Carcinoma

C. Total Neoadjuvant Therapy (TNT)

- High-risk LARC
- Need for better systemic control
- Desire to increase pathological complete response (pCR)
- Planning for non-operative “watch-and-wait” strategy
- TNT reduces systemic relapse risk and increases response rates

D. Clinical Complete Response (cCR) — Organ Preservation

- Patients achieving cCR after neoadjuvant therapy may be considered for **non-operative management** (watch-and-wait)

Colon Carcinoma

Neoadjuvant therapy is **not routine** for colon cancer

A. Locally Advanced Colon Cancer

- **T4b tumors** (invading adjacent organs)
- **Bulky tumors not easily resectable upfront**
- **Tumors with high risk of positive margins (R1/R2)**
- Benefit in **pMMR (proficient mismatch repair)** tumors.

B. dMMR / MSI-H Colon Cancer

- Neoadjuvant **immunotherapy** (e.g., PD-1 inhibitors) is emerging as a powerful option for:
- **Locally advanced MSI-H/dMMR colon cancer**
- High response rates, sometimes allowing organ preservation
- This is a major paradigm shift

Surgical Management

Surgery is the main curative option for early-stage disease

- Types of surgery depend on tumor location
- Aim:
  - Remove tumor completely
  - Preserve bowel function when possible

Surgical Advancements

Shift from open surgery to **minimally invasive techniques**

- **Laparoscopic surgery:**
  - Smaller incisions
  - Faster recovery
- **Robotic surgery:**
  - Enhanced precision
  - Better visualization
- Improves patient outcomes

Surgical Advancements:

- **Laparoscopic vs Robotic**
- Both are minimally invasive approaches
- **Robotic surgery advantages**:
  - Better dexterity
  - 3D visualization
  - Cost is higher
  - Limited availability in developing countries
- **Organ preservation: Watch-and-Wait** for complete responders
- Enhanced recovery pathways (ERAS)

Systemic Therapy

- **Standard regimens**:
  - **FOLFOX, FOLFIRI,XELOX**
- New combinations are improving survival : Bevacizumab
- Chemotherapy may be:
  - Neoadjuvant (before surgery)
  - Adjuvant (after surgery)

Systemic Therapy : What's New

- **Targeted therapy**:
- Anti-EGFR (RAS WT)
- BRAF inhibitors (V600E)
- HER2-targeted therapy
- **Immunotherapy**:
- Checkpoint inhibitors for **MSI-H/dMMR**
- Trials ongoing for MSS tumors

Immunotherapy

- Uses immune system to fight cancer
- Checkpoint inhibitors:
  - **Pembrolizumab, nivolumab**
- Highly effective in MSI-high tumors
- Some cases show remarkable tumor regression
- May reduce need for surgery in selected patients

AI in Treatment

- AI helps personalize treatment plans
- Predicts drug response
- Assists clinicians in decision-making
- Speeds up research and drug development

Precision Oncology

- Molecular subtyping guides therapy
- NGS panels for treatment selection
- ctDNA-guided adjuvant therapy decisions

Radiotherapy Updates

- Modern techniques: **IMRT, VMAT, IGRT**
- Total Neoadjuvant Therapy (TNT) in rectal cancer
- Better toxicity profile & improved local control

Future Directions in World

- AI + genomics for personalized treatment
- Expansion of immunotherapy to MSS CRC
- Liquid biopsy–driven treatment adaptation
- More organ-preserving approaches

Recent Advancements in Colorectal Cancer (CRC) in Bangladesh :

1. Improved Clinicopathological Understanding
2. Expansion of Colonoscopy & Histopathology Services
3. Introduction of Molecular Testing (MMR / MSI)
4. Growing Use of Immunohistochemistry (IHC)
5. Increasing Awareness of Risk Factors & Early Detection Needs
6. Strengthening Oncology Treatment Patterns

- Based on recent published data:
- **Better documentation** of CRC patterns and demographics
- **Wider availability** of colonoscopy and biopsy services
- **Routine use of IHC** for MMR/MSI testing
- **Introduction of molecular profiling** (MMR gene mutation analysis)
- **Improved treatment protocols** and toxicity monitoring
- **Growing awareness** of early detection and screening needs

What Bangladesh Has Achieved

- **A recent BSMMU-based study showed:**

- **34.9%** of CRC patients had MMR gene mutations
- MLH1 + PMS2 loss was the most common pattern
- MSI-H status strongly correlated with MMR mutations ($p = 0.025$)

This is a major step toward precision oncology in Bangladesh

Future Direction in Bangladesh

- Expand screening nationwide
- Increase public awareness
- Improve affordability of treatment
- Introduce AI tools in healthcare
- Strengthen cancer infrastructure

Some odds : Diagnostic & Treatment cost

IHC cost in Bangladesh:

Single IHC marker: ~৳3,000–৳5,000

MMR/MSI 4-marker panel: ~৳12,000–৳18,000

Large panels : may exceed ৳20,000—৳ 35,000 depending on the lab

NGS Availability in Bangladesh

Dr. Lal PathLabs — Clinical Exome Sequencing (৳38,775–৳44,385)

icddr,b Genome Centre — Full cancer NGS service (price not published but designed to be affordable)

NGS Cost Range: ৳38,000 – ৳45,000 (based on available data)

Targeted Therapy & Immunotherapy Cost in Bangladesh

Therapy Type	Drug	Verified Price (BD)	Estimated Monthly Cost
Targeted therapy	**Bevacizumab**	100 mg: ৳13,925–23,511; 400 mg: ৳48,500–79,586	৳60,000–100,000
Targeted therapy	**Cetuximab**	*No BD data* (regional estimate)	৳80,000–150,000 per dose
Targeted therapy	**Panitumumab**	*No BD data* (regional estimate)	৳90,000–160,000 per dose
Immunotherapy	**Pembrolizumab**	*No BD data* (regional estimate)	৳100,000–150,000 per cycle
Immunotherapy	**Nivolumab**	*No BD data* (regional estimate)	৳100,000–150,000 per cycle

Take-Home Messages

- CRC care is shifting toward **precision, personalization, and minimal invasiveness**
- **Molecular profiling** is **mandatory**
- Multidisciplinary coordination improves outcomes**(MDT Board)**
- Early detection remains the strongest tool
- **Bangladesh needs**:
  - Better access
  - Improved awareness
  - Strong healthcare policy support

Any Question ?


THANK
YOU

Screening of CRC

Screening Innovations

Risk-adapted screening strategies

Improved stool-based tests (FIT-DNA)

Focus on **early-onset CRC screening**

Screening of CRC :

Average risk:

Start 45 → FIT yearly / Colonoscopy every 10 years

Family history:

Start 40 or 10 years earlier → Colonoscopy every 5 years

IBD:

Start 8 years after diagnosis → Colonoscopy every 1–3 years

Lynch syndrome:

Start 20–25 → Colonoscopy every 1–2 years

FAP:

Start 10–12 → Annual endoscopy

First-Line Screening (Most Practical for Bangladesh)

A. 1. FIT (Fecal Immunochemical Test)
Every 1 year
Affordable, available, non-invasive
Best option for mass screening in Bangladesh
2. gFOBT (if FIT unavailable)
Every 1 year
Less sensitive, but still useful in rural areas
B. Second-Line Screening (Where Available)
1. Colonoscopy
Every 10 years
Gold standard
Recommended for urban centers (Dhaka, Chattogram, Sylhet)