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REKNIHT
CANCER

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COLORECTAL CANCER

Risk factors Colorectal Cancer & Current tends in Management of Rectal Cancer

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EDITORIAL

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Dear Doctor,

In **February** 2000, President Clinton officially dedicated **March** as National Colorectal Cancer Awareness Month. Since then March is celebrated world over as Colorectal Cancer Awareness day.

We are pleased to bring before you 4th issue of **"RETHINK CANCER"**. It enlighten on colorectal cancer- risk factors and current trends in management of rectal cancer. We hope that the 3rd issue on Risk Factors & Current trends in management of Ovarian Cancer was informative. It was well received by our obstetrician and gynaecological colleagues.

Rainy season is over. Festive season is ahead. We wish all our readers happy and prosperous Samvat 2075.

COLORECTAL CANCER

RISK FACTORS

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person's age or family history, can't be changed.

Dr. Viren A Shah

But having a risk factor does not mean that you will get the disease. And some people who get the disease may not have any known risk factors.

Researchers have found several risk factors that might increase a person's chance of developing colorectal cancer or colorectal polyps.

WHAT ARE THE RISK FACTORS?

- Obesity
- Smoking
- Colorectal Polyps
- Racial and ethnic group
- Factors with unclear effects
- Physical Inactivity
- Alcohol
- Inflammatory bowel disease
- Type 2 diabetes
- Diet
- Age
- Genetic factor
- Family history of colorectal cancer or adenomatous polyps

OBESITY

If you are overweight or obese, your risk of developing and dying from colorectal cancer is higher. Being overweight, especially having a larger waistline raises the risk of colon and rectal cancer in both men and women, but the link seems to be stronger in men.

PHYSICAL INACTIVITY

If you're not physically active, you have a greater chance of developing colon cancer. Being more active can help lower your risk.

DIET

A diet that's high in red meats, such as beef, pork, lamb, or liver and processed meats, like hot dogs and some luncheon meats raises your colorectal cancer risk.

Cooking meats at very high temperatures, frying, broiling, or grilling creates chemicals that might raise your cancer risk. It's not clear how much this might increase your colorectal cancer risk. It's not clear if other dietary components, for example, certain types of fats affect colorectal cancer risk.

SMOKING

People who have history of smoking for a long time are more likely than non-smokers to develop and die from colorectal cancer.

ALCOHOL

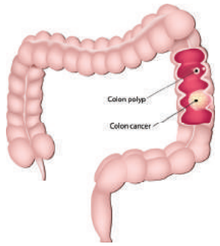
Colorectal cancer has been linked to moderate to heavy alcohol use. Limiting alcohol use to no more than 2 drinks a day for men and 1 drink a day for women could have many health benefits, including a lower risk of many kinds of cancer.

AGE

Your risk of colorectal cancer goes up as you age. Younger adults can get it, but it's much more common after age 50.

50+

COLORECTAL POLYPS OR COLORECTAL CANCER



If you have a history of adenomatous polyp, you are at increased risk of developing colorectal cancer. This is especially true if the polyps are large, if there are many of them, or if any of them show dysplasia.

If you've had colorectal cancer, even though it was completely removed, you are more likely to develop new cancers in other parts of the colon and rectum. The chances of this happening are greater if you had your first colorectal cancer when you were younger.

INFLAMMATORY BOWEL DISEASE

If you have inflammatory bowel disease (IBD), including either ulcerative colitis or Crohn's disease, your risk of colorectal cancer is increased.

IBD is a condition in which the colon is inflamed over a long period of time. People who have had IBD for many years, especially if untreated, often develop dysplasia. Dysplasia is a term used to describe cells in the lining of the colon or rectum that look abnormal, but are not true cancer cells. They can change into cancer over time.

If you have IBD, you may need to start getting screened for colorectal cancer when you are younger and be screened more often.

FAMILY HISTORY OF COLORECTAL CANCER OR ADENOMATOUS POLYPS

Most colorectal cancers are found in people without a family history of colorectal cancer. Still, nearly 1 in 3 people who develop colorectal cancer have other family members who have had it.

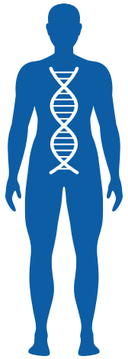
People with a history of colorectal cancer in a first-degree relative (parent, sibling, or child) are at increased risk. The risk is even higher if that relative was diagnosed with cancer when they were younger than 45, or if more than one first-degree relative is affected.

The reasons for the increased risk are not clear in all cases. Cancers can "run in the family" because of inherited genes, shared environmental factors, or some combination of these.

Having family members who have had adenomatous polyps is also linked to a higher risk of colon cancer.

GENETIC

About 5% of people who develop colorectal cancer have inherited gene changes that cause family cancer syndromes and can lead to them getting the disease.



The most common inherited syndromes linked with colorectal cancers are Lynch syndrome (hereditary non-polyposis colorectal cancer, or HNPCC) and familial adenomatous polyposis (FAP), but other rarer syndromes can increase colorectal cancer risk, too.

Lynch syndrome is the most common hereditary colorectal cancer syndrome. It accounts for about 2% to 4% of all colorectal cancers. In most cases, this disorder is caused by an inherited defect in either the MLH1 or MSH2 gene, but changes in other genes can also cause Lynch syndrome. These genes normally help repair DNA that has been damaged.

The cancers linked to this syndrome tend to develop when people are relatively young. People with Lynch syndrome can have polyps, but they tend to only have a few. The lifetime risk of colorectal cancer in people with this condition may be as high as 80%, but this depends on which gene is affected.

Familial adenomatous polyposis is caused by changes in the APC gene that a person inherits from his or her parents. About 1% of all colorectal cancers are caused by FAP.

In the most common type of FAP, hundreds or thousands of polyps develop in a person's colon and rectum, often starting at ages 10 to 12 years. Cancer usually develops in 1 or more of these polyps as early as age 20. By age 40, almost all people with FAP will have colon cancer if their colon hasn't been removed to prevent it.

RARE INHERITED SYNDROMES LINKED TO COLORECTAL CANCER

- **Peutz-Jeghers syndrome (PJS):** People with this inherited condition tend to have freckles around the mouth (and sometimes on their hands and feet) and a special type of polyp called hamartomas in their digestive tracts. These people are at a much higher risk for colorectal cancer, as well as other cancers, and they usually are diagnosed at a younger than usual age. This syndrome is caused by mutations in the STK11 (LKB1) gene.

- **MYH-associated polyposis (MAP):** People with this syndrome develop many colon polyps. These will almost always become cancer if not watched closely with regular colonoscopies. This syndrome is caused by mutations in the MYH gene (which is involved in "proofreading" the DNA and fixing any mistakes) and often leads to cancer at a younger age.

RACIAL AND ETHNIC BACKGROUND

African Americans have the highest colorectal cancer incidence and mortality rates. The reasons for this are not fully understood.

Jews of Eastern European descent (Ashkenazi Jews) have one of the highest colorectal cancer risks of any ethnic group.

TYPE 2 DIABETES

People with type 2 (usually non-insulin dependent) diabetes have an increased risk of colorectal cancer. Both type 2 diabetes and colorectal cancer share some of the same risk factors (such as being overweight and physical inactivity). But even after taking these factors into account, people with type 2 diabetes still have an increased risk. They also tend to have a less favourable prognosis after diagnosis.

FACTORS WITH UNCLEAR EFFECTS

Night shift work

Some studies suggest working a night shift regularly may increase the risk of colorectal cancer. It's thought this might be due to changes in levels of melatonin, a hormone that responds to changes in light. More research is needed.

PREVIOUS TREATMENT FOR CERTAIN CANCERS

Some studies have found that men who survive testicular cancer seem to have a higher rate of colorectal cancer and some other cancers. This might be because of the treatments they have received such as radiation therapy.

Several studies have suggested that men who had radiation therapy to treat prostate cancer might have a higher risk of rectal cancer because the rectum receives some radiation during treatment. Most of these studies are based on men treated in the 1980s and 1990s, when radiation treatments were less precise than they are today. The effect of more modern radiation methods on rectal cancer risk is not clear.

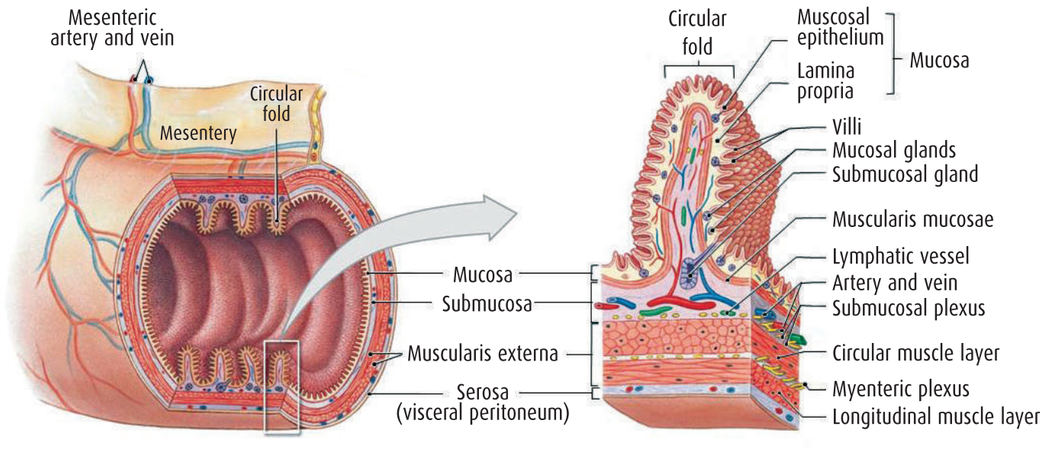
COLORECTAL CANCER STAGING

Treatment for rectal cancer is based on the stage of the disease when diagnosed.

Dr. Himanshu Mehta
(Onco Pathologist)

HOW IS THE STAGE DETERMINED?

The staging system most often used for colorectal cancer is the American Joint Committee on Cancer (AJCC) **TNM** system.



The system described below is the most recent AJCC system effective January 2018. It uses the pathologic stage (also called the surgical stage)

AJCC Stage	Stage grouping	Stage description
0	Tis, N0, M0	Carcinoma in situ or intramucosal carcinoma (Tis). It has not grown beyond the mucosa
I	T1 or T2, N0, M0	The tumour has grown through the muscularis mucosa into the submucosa (T1), and it may also have grown into the muscularis propria (T2). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIA	T3, N0, M0	The tumour has grown into the outermost layers of the colon or rectum but has not gone through them (T3). It has not reached nearby organs. It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIB	T4a, N0, M0	The tumour has grown through the wall of the colon or rectum but has not grown into other nearby tissues or organs (T4a). It has not yet spread to nearby lymph nodes (N0) or to distant sites (M0).
IIC	T4b, N0, M0	The tumour has grown through the wall of the colon or rectum and is attached to or has grown into other nearby tissues or organs (T4b). It has not yet spread to nearby lymph nodes (N0) or to distant sites (M0).
IIIA	T1 or T2, N1/N1c, M0	The tumour has grown through the mucosa into the submucosa (T1), and it may also have grown into the muscularis propria (T2). It has spread to 1 to 3 nearby lymph nodes (N1) or into areas of fat near the lymph nodes but not the nodes themselves (N1c). It has not spread to distant sites (M0).
	OR	
	T1, N2a, M0	The tumour has grown through the mucosa into the submucosa (T1). It has spread to 4 to 6 nearby lymph nodes (N2a). It has not spread to distant sites (M0).
IIIB	T3 or T4a, N1/N1c, M0	The cancer has grown into the outermost layers of the colon or rectum (T3) or through the visceral peritoneum (T4a) but has not reached nearby organs. It has spread to 1 to 3 nearby lymph nodes (N1a or N1b) or into areas of fat near the lymph nodes but not the nodes themselves (N1c). It has not spread to distant sites (M0).
	OR	
	T2 or T3, N2a M0	The tumour has grown into the muscularis propria (T2) or into the outermost layers of the colon or rectum (T3). It has spread to 4 to 6 nearby lymph nodes (N2a). It has not spread to distant sites (M0).
	OR	
	T1 or T2 N2b M0	The cancer has grown through the mucosa into the submucosa (T1), and it may also have grown into the muscularis propria (T2). It has spread to 7 or more nearby lymph nodes (N2b). It has not spread to distant sites (M0).
IIIC	T4a, N2a, M0	The tumour has grown through the wall of the colon or rectum (including the visceral peritoneum) but has not reached nearby organs (T4a). It has spread to 4 to 6 nearby lymph nodes (N2a). It has not spread to distant sites (M0).
	OR	
	T3 or T4a, N2b M0	The tumour has grown into the outermost layers of the colon or rectum (T3) or through the visceral peritoneum (T4a) but has not reached nearby organs. It has spread to 7 or more nearby lymph nodes (N2b). It has not spread to distant sites (M0).
	OR	
	T4b, N1 or N2, M0	The tumour has grown through the wall of the colon or rectum and is attached to or has grown into other nearby tissues or organs (T4b). It has spread to at least one nearby lymph node or into areas of fat near the lymph nodes (N1 or N2). It has not spread to distant sites (M0).
IVA	Any T, Any N M1a	The tumour may or may not have grown through the wall of the colon or rectum (Any T). It might or might not have spread to nearby lymph nodes. (Any N). It has spread to 1 distant organ (such as the liver or lung) or distant set of lymph nodes, but not to distant parts of the peritoneum (the lining of the abdominal cavity) (M1a).
IVB	Any T, Any N, M1b	The tumour might or might not have grown through the wall of the colon or rectum (Any T). It might or might not have spread to nearby lymph nodes (Any N). It has spread to more than 1 distant organ (such as the liver or lung) or distant set of lymph nodes, but not to distant parts of the peritoneum (the lining of the abdominal cavity) (M1b).
IVC	Any T, Any N, M1c	The tumour might or might not have grown through the wall of the colon or rectum (Any T). It might or might not have spread to nearby lymph nodes (Any N). It has spread to distant parts of the peritoneum (the lining of the abdominal cavity), and may or may not have spread to distant organs or lymph nodes (M1c).

MANAGEMENT OF CARCINOMA RECTUM

Dr. Shakuntala Shah
(Surgical Oncologist)

I. DIAGNOSTIC:

DIGITAL RECTAL EXAMINATION - DRE

- **What is Digital Rectal Examination- DRE?**

  To assess type of tumour, site of tumour and relation to surrounding structures- bladder, lateral pelvic walls, sacrum, in male-prostate, in female-posterior vaginal wall

- **Type of tumour-**

  1. Polypoidal, frond like or villous,

  2. Ulcerative with indurations' and invasive to surrounding structures causing fixity or exophytic nodular mass

- **Site-**

  On DRE the approximate distance of lower border of lesion is taken from the anal verge- making it low rectal, mid rectal or high rectal. This is important for sphincter preserving surgery.

II. IMAGING:

- X-ray chest
- MRI for local staging- It shows the rectal wall thickness involved, para rectal spread of the disease and nodes
- CT Scan- To rule out liver metastasis and spread to retroperitoneal node
- PET CT- Indicated only in locally advanced disease where chances of systemic disease are high. That changes the intent of treating, whether curative or palliative.
- Endorectal ultrasound is now also available for staging of rectal cancer.
- **Colonoscpy** - To rule out synchronous lesion or polyps in colon

III. TREATMENT:

1. Surgery-

- Sphincter preserving anterior resection is the treatment of choice and ultra low anterior resection can also be done to preserve the anal sphincter, where the distal margin is anal canal and colo-anal anastomosis is performed.
- The crux of surgery is at least 5 cms of mesorectal clearance, wide circumferential margins, and minimum 2 cms free distal margin of resection. The goal is to prevent local recurrence.
- Now a days surgical approach may be by minimal invasive surgery- laparoscopic or robotic.

2. Pre operative neo adjuvant treatment-

- The treatment is chemotherapy with radiation. This is required for any tumour which has crossed rectal wall into meso-rectum, nodal involvement or involvement of plane between prostate and rectum in male, and vagina and rectum in female.

3. Surgery for colorectal liver metastasis-

- Surgery is feasible when 2-3 cms metastasis, 3-5 in number are present.
- When liver metastasis is present during primary diagnosis they are excised after NACRT, synchronously with primary surgery.
- When liver metastasis present after primary treatment, they can be excised if they are 2-3 cms and 3-5 in numbers at the time of diagnosis on followup.
- Other methods of ablating single small metastasis are by RFA or stereotactic radio surgery.

4. Palliative Surgery-

- If tumour is not operable, and the tumour is obstructing the colon, then palliative surgery either colostomy or stent placement has to be considered, depending on the life expectancy.

APPROACH CONSIDERATIONS

A multidisciplinary approach that includes surgery, medical oncology, and radiation oncology is required for optimal treatment of patients with rectal cancer.

Staging and treatment:

Stage 0: Polypectomy / Local excision/ Trans-anal resection.

Stage I: For stage I cancer, surgery is usually the main treatment. Some small stage I cancers can be removed through the anus, using transanal resection or transanal endoscopic microsurgery (TEM). For other cancers, a low anterior resection (LAR), proctectomy with colon-anal anastomosis, or an abdominoperineal resection (APR) may be done, depending on exactly where the cancer is located within the rectum.

Stage II: For stage II rectal cancer is treated with chemotherapy, radiotherapy and surgery, although the order of these treatments might differ individually.

Stage III: For stage III rectal cancer will be treated with chemotherapy, radiation therapy and surgery.

Stage IV: Treatment options for stage IV disease depend to some extent on widespread of the cancer.

- These patients are treated with chemotherapy, followed by surgery to remove the rectal tumour and distant tumours- if they are 2-3 cms and 3-5 in numbers at the time of diagnosis, and usually followed by chemotherapy and radiation therapy (chemo radiation)
- If the cancer is more widespread and can't be removed completely by surgery, treatment options depend on whether the cancer is causing obstruction of bowel or not. If it is, surgery might be needed for palliative procedure. If not, the cancer will likely be treated with chemotherapy and/or targeted therapy drugs.

CHEMOTHERAPY REGIM FOR RECTAL CANCER

- FOLFOX: 5-FU, Leucovorin, and Oxaliplatin
- FOLFIRI: 5-FU,Leucovorin, and Irinotecan
- CAPOX: Capecitabine and Oxaliplatin
- FOLFOXIRI: 5-FU,Leucovorin, Oxaliplatin, and Irinotecan
- One of the above combinations, plus either a drug that targets VEGF (Bevacizumab, Ziv-aflibercept, or Ramucirumab, or a drug that targets EGFR (Cetuximab or Panitumumab)
- 5-FU and leucovorin, with or without a targeted drug
- Capecitabine, with or without a targeted drug
- Irinotecan, with or without a targeted drug
- Cetuximab alone
- Panitumumab alone
- Regorafenib alone
- Trifluridine and tipiracil (Lonsurf)

The choice of regimens depends on several factors, including any previous treatments, overall health of patient, and how well patient can tolerate treatment.

If the only site of cancer metastasis is the liver, it might be treated with hepatic artery embolisation. This may shrink the tumour in the liver better than if the chemotherapy is given intravenously or/and orally.

RADIATION TREATMENT FOR RECTAL CANCER

Dr. Samrendra Das
(Radiation Oncologist)

History of Radiation therapy in Rectal Cancer

- Local recurrence rates were higher after resection
- Phase III trials have shown significant improvement in local recurrence with addition of radiotherapy (Pre op/Post op)
- Both long course/short course RT acceptable

Advantages of preoperative RT/CT

- Better compliance
- Down staging of the disease
- Increased respectability- especially in T4 lesion
- Maintenance or improvement in quality of life
- Good chances of sphincter preservation
- Chance of preservation of bladder function and sexual function
- Complete pathological response in 10%-20% of patients

Disadvantages of preoperative RT

- Staging depend on- CT,MRI,EUS
- Loss of prognostic information on nodes
- Over treating patients with early disease and undected metastasis

Short course radiotherapy

- 5Gy x5#- total 25Gy in one week ⇨ gap of 1 week ⇨ Surgery ⇨ Adjuvant chemotherapy if node positive
- Or 25Gy in one week⇨gap of 4-8 weeks ⇨ Surgery

Advantages

- Similar toxicity profile as compared to long course
- Greater convenience
- Low cost
- Patient preference
- Logistic advantage for high burden centre
- Systemic treatment post operatively can be initiated early

Disadvantages

- Cannot be used incT4 lesion
- Chronic toxicity may be higher

Long course radiotherapy

45 Gy 25# or 50.4 Gy 28# with5 Fu based chemotherapy ⇨ gap of 4-8 weeks ⇨ Surgery ⇨ 5Fu based adjuvant chemotherapy

Advantages

- Can be given in both Perop/Postop settings
- cT4 lesion can also be treated

Disadvantges

- Systemic treatment is delayed

Conclusion of short course and long course radiotherapy

- No significant difference in local recurrence rate
- In terms of acute toxicity- Acute toxicity higher in long course radiotherapy compared to short course radiotherapy
- Long term toxicity- no statistically significant differences in long course or short course radiotherapy
- No difference in efficacy and long term toxicities in resectable disease

Mrs. Namita Paritosh Kohok,
Mrs United Life Time Queen 2017

Public lecture on Impact of Breast Cancer on our society at Hubballi, Karnataka

Inaugurated Radon Cancer Centre, Hubballi, Karnataka with Padmashri Dr. R.B.Patil-Founder of Karnataka Cancer Therapy & Research Institute

Mrs. Priya Sunil Dutt, Managing Trustee Nargis Dutt Memorial Charitable Trust