Rectal cancer: A review
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Introduction
Rectal cancer is one of the major health problems of the Westernized World. It is the 3rd most diagnosed malignancy accounting for 10% to 15% of newly diagnosed cancers in Europe and United States.1,2,3,4. It is a dynamically changing diseases entity.5,6. It's incidence varies from place to place and occurs most frequently in the population with the highest standard of living excepting Japan7, North America, Australia, New Zealand, North & West Europe have a very high incidence of the disease.8 In USA, it's incidence rate increased from mid 1970 through 1992, decreased from 1992 to 1995 and stabilized from 1996 to 2000.9. But there is no Central Cancer Registry in our country. Both Population Based & Hospital Based Cancer Registry are yet to develop. So, it is difficult to define the exact picture of rectal cancer prevailing among the population of our country. Only the Oncology Department of different Medical College Hospitals & Institutes have just started to maintain the registry of cancer patient attending the department. But the standard of documentation is not up to the mark. Again all the Oncology Departments are not provided with radiotherapy machines. So the figures vary from centre to centre mainly due to the biasness of radiotherapy. For that reason, colorectal cancer accounted for 2.06% of all the cancers among the patients attending the Department of Radiotherapy, Dhaka Medical College Hospital whereas it accounted for 7.36% among those attending the Department of Radiotherapy of Sher-E Bangla Medical College Hospital10,11,12.

Epidemiology

Gender
There is no conclusive evidence of sex predominance. Both sexes can be equally affected8. But in majority of the cases male predominance slightly over female13.

Age
Rectal cancer is the disease of elderly people and the peak incidence is in the 7th decade of life.14. Less than 20% cases are diagnosed in persons under 50 years of age, It is rare in adolescents and young adults15-16. Only a few cases have been reported in children17. But this scenario is just reverse in our country due the reasons yet to be find out. In a study done by the author as a principal investigator over 102 rectal cancer patients from 1994 to 2002 titled "Rectal Cancer- Experience with 102 cases" (accepted for publication in The Journal of Teachers Association of Sir Salimullah Medical College, also presented as a Scientific Paper in the Conference of Asian Clinical Oncological Society in Seoul, Korea, 2003) patients aged between 10 and 92 years, Mean age at diagnosis was only 43.38 years, 52.94% aged within 40 years. Three patients were of pediatric age group.

Race
The incidence of colorectal cancer has increased by 30% in blacks since 1973 and is now higher than in whites18.

Etiology
Not definitely known, but the following factors are found to be associated with this cancer:

Environment
Asians, Africans and South Americans have low incidence of colorectal cancer. But when they migrate to North America, they suffer more from this type of cancer. Environment has been blamed for this higher incidence18.
Diet
Diet rich in fat and cholesterol have been linked to an increased risk of colorectal cancer. Dietary fat causes endogenous production of secondary bile acids, neutral steroids and increases bacterial degradation of these acids & steroids, thereby promoting carcinogenesis. Historically, diet rich in cereal fiber, bran, yellow or green vegetables are said to have a protective effect.

Genetic factor
There are groups that have a very high incidence of colorectal cancer. These groups include those with hereditary conditions such as; familial polyposis, hereditary nonpolyposis, Lynch Syndrome of variant I & II, ulcerative colitis. Together they account for 10% to 15% of colorectal cancers. More common conditions with an increased risk are; personal history of colorectal cancer, previous operation -even cholecystectomy, first degree family history, previous history of ovarian, endometrial and breast cancer. These high risk groups account for 23% of all colorectal cancer.

Signs & symptoms
Patients with rectal cancer may present with change in bowel movements; rectal fullness, urgency, tenesmus, bleeding per rectum. Pelvic pain indicates advanced stage of the disease and is due to local extension of the tumor to the pelvic nerve. Symptoms due to metastatic spread depends upon the sites of deposit.

Screening and Diagnosis
Fecal occult blood test: It is inexpensive, but have been associated with many false positive and false negative results. About 50% of the colorectal cancer goes undetected, they are not bleeding at the time of the test.

Digital rectal examination
Simple to perform and can detect lesions up to 7 centimeters from the anal verge.

Sigmoidoscopy
Flexible proctosigmoidoscopy is safe and more comfortable than examination with a rigid proctoscope. Colonoscopy is for exclusion of associated colonic growth.

Barium enemas
Here again the problem of 2% to 61% false negative findings due to poor preparation and difficulties in detecting smaller lesions.

Biopsy
Biopsy of the detectable lesion is essential for confirmation of diagnosis. It is safe and easy to take the biopsy endoscopically.

Investigations for staging and treatment
- Chest X-ray to confirm/exclude any metastatic deposits.
- CT-Scan/MRI of abdomen and pelvis.
- Trans rectal ultrasonography.
- Complete blood count including platelet count.
- Liver and renal function tests
- Urine analysis
- CEA

Cellular classification
Adenocarcinoma: Constitutes 90% to 95% of rectal cancer. They may present with multiple degrees of differentiation and variable amount of mucin. Mucinous variant is characterized by huge amount of extracellular mucin in the tumor with the tendency to spread within the peritoneum. It is commonly seen in younger patients having less favourable prognosis. Signet ring cell type, an uncommon variant contains large quantities of intracellular mucin causing the displacement of cytoplasm and nucleus. They involve the submucosa making difficulties in diagnosis with conventional imaging techniques.

Other variants
Are scirrhous type, squamous cell carcinoma, adenosquamous carcinoma, undifferentiated
carcinoma, neuroendocrine and carcinoid tumors. Sarcoma accounts for 0.1% to 0.3% of all rectal cancers and melanomas are rare.

**Stage information**

Treatment decisions should be made with reference to the TNM classification rather than older Duke's or the Modified Astler-Coller (MAC) classification schema\(^\text{23}\).

**TNM definitions**

*Primary tumor (T)*
- TX: Primary tumor can not be assessed
- TO: No evidence of primary tumor
- Tis: Carcinoma in situ: intraepithelial or invasion of the lamina propria. It includes cancer cells confined within the glandular basement membrane or lamina propria (intramucosal) with no extension through the muscularis mucosa in to submucosa.
- T1: Tumor invades submucosa.
- T2: Tumor invades muscularis propria.
- T3: Tumor invades through the muscularis propria in to the subserosa or in to nonperitonealized pericolic or perirectal tissues.
- T4: Tumor directly invades other organs or structures, and/or perforate the visceral peritoneum.

*Regional lymph nodes (N)*
- NX: Regional lymph nodes can not be assessed.
- NO: No regional lymph node metastasis
- N1: Metastasis in 1 to 3 regional lymph nodes.
- N2: Metastasis in 4 or more regional lymph nodes.

*Distant metastasis (M)*
- MX: Distant metastasis can not be assessed.
- MO: No distant metastasis
- M1: Distant metastasis.

**Stage 0**
- Tis, NO, MO

**Stage 1**
- T1, NO, MO

**Stage II**
- T2, NO, MO
- T3, NO, MO
- T4, NO, MO

**Stage III**
- Any T, N1, MO
- Any T, N2, MO

**Stage IV**
- Any T, Any N, M1.

**Treatment option overview**

Colorectal cancer is a highly treatable and often curable disease when diagnosed and treated early. Marked advances have been noticed in the management of this disease in the Western Society\(^\text{8}\). Here death rates have been declining for both whites and blacks\(^\text{24}\). Followings are the treatment options:

**Surgery**

The most effective option of rectal cancer is surgical resection of the primary and regional lymph nodes for localized disease\(^\text{18}\). The technique of rectal excision has impact upon the rate of local recurrence. Meticulous surgical resection with at least 2 centimeters distal surgical margin including node bearing mesorectum has reduced the rate of local recurrence. The major limitations of the surgery are: presence of sphincter in the lower end of rectum which controls defecation and the inability to obtain a radical margins because of the presence of bony pelvis. However, the surgical procedures are:

**Resection anastomosis**

This is the preferred method of surgery. Here resection of the primary with adequate free margin including resection mesorectum and anastomosis (colorectal or coloanal anastomosis) are done. But the growth should be at least 6-7 cms above the anal verge. Here anal sphincter is preserved and colostomy is avoided -thus providing with a better quality of life.

**Abdominoperineal resection (APR)**
When the growth is within 6 cms from anal margin or the growth is bulky one, resection anastomosis can not be done. APR is the appropriate surgical option in this situation. The patient will have to bear the burden of permanent colostomy. Care is given to preserve the autonomic nerve, thus minimizing the bladder and sexual function morbidity.

Local excision
Trans anal local excision is only recommended in T1 well to moderately differentiated rectal cancer with out histologically proven lympho vascular involvement, provided that a full thickness negative margin may be achieved. Pre operative trans rectal ultrasonogram is helpful in defining lesions that can be resected satisfactorily by local excision.

Aggressive surgery
Partial or total pelvic exenteration is uncommon situation, where bladder, uterus, vagina or prostate are invaded.

Palliative surgery
Surgical resection/ anastomosis or bypass of obstructing lesions in selected cases or resection for palliation are done in selected advanced cases. Surgical resection of isolated metastases in lung, liver and ovaries can be done for palliation.

Adjuvant therapy
Approximately 75% of the patients with rectal cancer present at a stage when all the gross tumor can be surgically resected. Nevertheless, despite the high resectability rate, almost half of all the patients will die from metastatic disease, primarily because of the residual disease that is not apparent at the time of surgery. These individuals are the candidate for local or systemic adjuvant therapy. Usually the patients of real Stage-I with wide surgical resection do not need adjuvant therapy. Mainly the patients of Stage-II & III become benefited from adjuvant therapy.

Radiotherapy
Mainly used as adjuvant therapy in Stage -II & III rectal cancer to reduce the locoregional recurrence. Here the primary and the regional nodal areas are irradiated. Usually 50 to 55 Gys are given by conventional fractions. In most trials, adjuvant radiotherapy alone have shown to decrease the local recurrence but without definite effect on survival. Radiotherapy is used in selected advanced cases for palliation of local symptoms. Pain is decreased in 80% of the irradiated patients, control of bleeding in 70% cases. But obstruction is difficult to be relieved by radiation. Endocavitory brachytherapy with or without external beam radiation can give results equivalent to surgery in selected patients of Stage-I with tumors less than three centimeters, well differentiated, without deep ulceration.

Chemoradiation
Means radiotherapy along with simultaneous chemotherapy. These combined modalities are the best post operative adjuvant therapy. They result in local failure rates lower than with either radiation therapy or chemotherapy alone.

Neo-adjuvant therapy
Therapy given before surgery, specially in advanced (T3 & T4) rectal cancer. These cases are difficult to be managed by surgery. Pre operative neo-adjuvant therapy (radiotherapy with or with- out chemotherapy) regresses the tumor, thus making them operable. Sphincter can be preserved by neo- adjuvant therapy in selected cases when the tumor located near to the anal sphincter.

Chemotherapy
Main treatment for advanced and recurrent rectal cancer is palliation with 5-Flourouracil based chemotherapy. Chemotherapy is also given along with radiation as adjuvant in Stage-II & III and neoadjuvant to surgery in locally advanced cases. Response has been improved...
but with a variable effect on survival when modulated by leucovorin or methotrexate. Randomized clinical trials show that alpha interferon appears to add toxic effects but no clinical benefit to 5-Flurouracil therapy. Continuous infusion of 5-Flurouracil have resulted in increased response rates in some studies, with a modest benefit in median survival. Oral regimens using pro drugs of 5-Flurouracil pharmacologically stimulate continuous infusion and under clinical evaluation. Irinotecan is now standard therapy for patients with Stage-IV disease who do not respond to or progress on 5-FU. Oxaliplatin alone or combined with 5-FU and leucovorin has shown promising activity in previously treated and untreated patients and in patients with 5-FU refractory disease.

Follow up
Following completion of treatment, periodic evaluation is an integral part of rectal cancer management. It helps in identification and management of any recurrent disease. In our country majority of the patients present in advanced stage of the disease, so curative therapy can not be given. We have also limitation in expert manpower and machinaries for diagnosis & treatment of rectal cancer. Coordinated treatment approach, regular follow up provision and proper documentation system are to be developed. In conclusion we want to say that though rectal cancer is highly treatable and often curable when diagnosed and treated early, yet it is highly expensive in Bangladeshi perspective. So measures to be taken for prevention and early detection. People should be encouraged in taking sufficient vegetables, fruits and abstained from smoking, alcohol intake. Chemoprevention to be aimed for blocking the actions of carcinogens on the cells before the appearance of cancer. The most well studied agents in prevention of colorectal cancer includes; antioxidants, vitamin-C, vitamin-E; calcium, nonsteroidal anti-inflammatory drugs.

References
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