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Review Article

Minimizing locoregional recurrences in colorectal cancer surgery

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ABSTRACT

Colorectal cancer is a major cause of morbidity and mortality worldwide. The Indian scenario also shows a similar trend, and this has been attributed to the changing dietary patterns. Recurrence in colorectal cancer is associated with many factors, some related to the tumor itself and some to the surgical principles applied. Understanding these factors and application of sound surgical principles can go a long way in decreasing the incidence of colorectal cancer. Here, we highlight the main biological and technical factors implicated in the recurrence of colorectal cancer.

1. Introduction

Colorectal cancer is the third most common cancer in men and the second most common cancer in women worldwide. Almost 55% of the cases occur in more developed regions of the world. There is a wide geographical variation in incidence across the world, and the geographical patterns are very similar in men and women.

Mortality is higher in the underdeveloped than in the developed countries. The incidence in India is relatively lower than that in countries like China, Japan, and Indonesia.

In the Indian scenario, colorectal cancer stands fourth in men and third in women with respect to age-standardized incidence and mortality rates.[1]

SEER database reports that the overall 5-year survival for all cases of colorectal cancer is about 65%.[2]

Colorectal cancers present as localized disease in 39%; 36% present with involvement of the regional lymph nodes and 20% with metastatic disease. The 5-year survival in patients of colorectal cancer ranges from 90% in those with localized disease to 13% in those with distant disease.

Colorectal cancer is most frequently diagnosed among people aged 65–74 years (median age 68). Colorectal cancer

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deaths are the highest among people aged 75–84 years (median age 73).

2. Recurrent disease

Recurrence of disease occurs in about 30–50% of cases. The incidence of recurrence after curative resection for colorectal cancer is about 9.9% at 1 year, 26.2% at 3 years, and 31.5% at 5 years. Five-year recurrence rates range from 9.3% for stage I tumors to 56.1% for stage III disease. Locoregional recurrence occurs in 12.8% of patients at 5 years, and distant metastases occur in 26% of patients at 5 years. Distant sites of disease include the liver in 45%, lung in 10%, brain in 2%, bone in 2%, and other sites in 4%.[3]

Historically, the highest rate of recurrences was seen within the first 2 years, but the median time to recurrence is increasing, especially for rectal cancers, and surveillance beyond 5 years may be necessary. The incidence of local recurrence is also higher for rectal cancers as compared to colonic malignancy.[4,5]

The risk factors associated with recurrence of colorectal cancer may either be tumor related or technical.

The various tumor-related factors include

1) Stage of the disease
2) Grade of the tumor
3) Location of the tumor
4) Obstruction or perforation
5) Venous invasion
6) Perineural invasion
7) Low microsatellite instability
8) Diminished stream immune reaction
9) Aneuploidy
10) Mutant p53 gene expression

The single most important factor that affects the recurrence and survival is the stage of the tumor. The risk is greatest when the tumor has invaded beyond the confines of the bowel wall (T3 to T4) or involves nodes (N+) and is highest in patients with both.[6] The 5-year survival of patients with stage I disease is >90%, whereas for stage IV, it is <10%.

The two-tier system advocated for colorectal cancer grading is accepted by most pathologists today. It takes gland formation into account and defines high-grade tumors as the ones with <50% gland formation. Signet cell cancer is a relatively rare form of colorectal cancer. It is associated with a higher stage of the tumor at the time of diagnosis, coupled with high incidence of peritoneal seeding and overall poorer prognosis.[7]

Tumors located lower down and anteriorly in the rectum are associated with a higher incidence of local recurrence. The close anterior relation of the rectum to bladder and seminal vesicles in males, and uterus and vagina in females has been attributed to this.

Perforated colorectal cancer has been associated with higher rate of recurrence and lower overall survival, as shown by Cheynel et al.[8]

Lymphovenous invasion has been attributed with a higher incidence of local recurrence.[9]

Perineural invasion (PNI) has been studied of late as a prognostic factor in colorectal cancer. The 5-year disease-free survival rate was fourfold greater for patients with PNI-negative tumors versus those with PNI-positive tumors (65% vs 16%). The 5-year overall survival rate was also better in PNI-negative tumors versus PNI-positive tumors (72% vs 25%).[10]

Microsatellite instability (MSI) in colorectal cancers is associated with right colonic lesions, and is more often of the mucinous, signet ring cell or medullary histologic type, poorly differentiated, and have a brisk lymphocytic infiltrate. MSI-high tumors are associated with longer survival than either MSI-low or microsatellite-stable tumors, both in HNPCC and in sporadic cases, despite being often poorly differentiated. The presence of low MSI is associated with a higher rate of recurrence. The presence of tumor-infiltrating lymphocytes has been reported as a favorable prognostic factor.[11]

P53 gene mutation has been proven to be an adverse prognostic factor on the overall survival. The p53 mutation increases the risk of death by 2.82 times in patients with stage II and by 2.39 times in patients with stage III colon carcinoma.[12]

Technical factors mainly involve the adequacy of resection margins (radial, distal, and mesorectal) irrespective of the surgical method used. Since technical factors play a significant role in the recurrence rate, Nelson et al.[13] proposed certain surgical guidelines for the treatment of colorectal cancer.

3. Surgical guidelines

The present surgical guidelines state that for colonic malignancy lymphadenectomy should extend to the level of the origin of the primary feeding vessel, and suspected positive lymph nodes outside the standard resection should be removed when feasible. Bowel margins of more than 5 cm, both proximally and distally, should be obtained.

For rectal malignancy, an ideal bowel margin of 2 cm distally and 5 cm proximally, measured fresh with the use of full thickness, has been advised. The minimally acceptable distal margin for sphincter preservation is taken as 1 cm. Lymphovascular resection of the rectum should include a wide anatomic resection of the mesorectum, including the mesorectal fascia propria and 4 cm of clearance distal to the tumor and proximal ligation of the primary feeding vessel. Extended lateral lymphatic dissection is not supported based on the current evidence.

Certain principles common for both colon and rectal cancers are En bloc resection should be performed for tumors adherent to local structures; inadvertent bowel perforation should be avoided as it increases the risk of recurrence; thorough abdominal exploration for metastatic and locally advanced primary and lymph node disease should be performed.

Height of the tumor from anal verge also has an impact on the rate of recurrence. The tumors below the peritoneal reflection tend to be more infiltrative locally and are subjected to poorer intraoperative exposure and manipulation. The incidence of recurrence decreases as the height increases from the anal verge, with lower 1/3 tumors having a recurrence of 10–15%, middle 1/3 having 5–10%, and upper 1/3 rectal tumors