Can Radical Surgery Improve Survival in Colorectal Cancer?

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Prospective, randomized trials that study the best surgical technique to prevent local and distal metastases in colorectal cancer have not yet been performed. Prevention of local recurrence must be a major effort achieved by radical resection of the tumor area, by minimizing the possibility of suture line recurrence and of tumor remnants in intramesenteric lymph nodes or surrounding tissue, and by avoiding spillage of tumor cells. Extended resections of mesenteric lymph nodes or pelvic lymphadenectomy did not prove to be of significant benefit in most retrospective studies. In the case of adjacent organ involvement, en bloc resection is indicated since long-term survival can be obtained. This operation can be performed with low operative mortality rates even in the case of pancreas or duodenum involvement as is shown in our series of 34 patients (3% operative mortality). Frozen sections of the resection area have to be included in the operative procedure. For prevention of distant metastases, the no-touch technique of Turnbull should be performed. In a prospective, randomized trial of 236 patients operated on for colon cancer, liver metastases appeared later and to a lesser degree in patients operated on with the no-touch isolation technique, particularly in the case of angioinvasive growth of the tumor.

Resection of the primary malignant tumor in cancer of the colon and rectum is the treatment of choice since it offers the only possibility for cure. In the last few decades, survival has improved slightly, probably due to increased resectability rates and decreased direct postoperative mortality [1-3]. So far, prolongation of survival has not been obtained with other therapies. Studies with adjuvant chemotherapy, radiotherapy, and immunotherapy have not warranted routine use of these treatments, although one study recently reported a lower recurrence rate for rectal cancer when surgery alone was compared to surgery with postoperative irradiation and chemotherapy (55% and 33%, respectively) [4]. It is surprising that although surgery is the primary choice of treatment, few studies evaluating various surgical techniques have been performed. Many questions regarding the best surgical therapy in colon cancer still have to be answered, such as the optimal extent of resection, and the relevance of intraoperative techniques that avoid seeding of cancer cells. Furthermore, too many surgeons regard involvement of adjacent organs incurable, which may cause unnecessarily low resectability rates. Some form of fixation of the primary tumor to surrounding tissue exists in 10–40% of patients, which is not caused by tumor growth in the majority of cases [5-11]. Surgical therapy should relieve the patients of symptoms caused by the primary tumor and improve prognosis by avoiding the occurrence of local and distal metastases. It would be of utmost importance to establish prior to operation what the chances are for local or distal recurrences in order to adjust surgical therapy to the risk of recurrence.

Prognosis

Prognosis in colon cancer depends on a few variables, primarily the Dukes’ classification. Most of the studies find a correlation between survival and the Dukes’ classification. The classical Dukes’ staging system refers to Dukes’ A as a tumor confined to the bowel wall, Dukes’ B as an extension outside serosa and/or peri-rectal fat, and Dukes’ C as either A or B with lymph node metastases. Stage D was added at a later date indicating infiltrative growth in adjacent organs or distant metastases. Other prognostic variables are not consistently found. In a total number of 350 patients who participated in 2 multicenter trials on colon cancer from 1979 to 1981 in the Netherlands [12] the following prognostic variables were found: patients with tumors of a diameter between 3.5 and 6 cm had a poor survival rate in comparison to those patients with small (<3.5 cm) and very large tumors (p = 0.02). Ulcerative growth was associated with a poor prognosis as was angioinvasive growth. Poorly differentiated tumors did worse than moderately and well-differentiated tumors. Prognosis appeared to be strongly related to Dukes’ staging and to central node involvement. Localization of the primary tumor and age did not correlate with survival.

Most authors describe the prognostic value of pathological grading of the tumor [13-15]. Future studies will have to show whether relatively new techniques such as computed tomographic scan and intrarectal ultrasound in combination with the above-mentioned parameters can predict the risk of recurrence before operation. Information obtained by preoperative biopsies together with knowledge of the shape and size of the tumor in the bowel wall, established by intrarectal ultrasound, may provide a preoperative staging system.

The Role of Surgery

Realizing that surgical resection is the most important therapeutic modality in colorectal cancer, what do we hope to
accomplish with surgical resection and what do we consider to be the best surgical technique? The purpose of surgery in primary colon cancer is relief of morbidity and prevention of mortality by local recurrence and distant metastases. Relief of complaints can be accomplished by simple removal of the tumor area alone but excision of the tumor-containing bowel segment is probably not sufficient and will lead to a high local recurrence rate. Currently, there is still no standard procedure that describes the optimal extent of bowel resection and dissection of lymph node-containing mesentery since prospective, randomized studies have not been performed. In theory it should be possible to avoid local recurrence by radical removal of the tumor and involved lymph nodes and by prevention of tumor spillage, which is of particular importance in cases of fixation of the tumor to adjacent tissues. It is conceivable that surgery is much more effective in preventing local recurrence than distant metastases; however, prevention of local recurrence is only relevant for survival if this form of recurrence occurs separately from systemic dissemination.

Local Recurrence

Local recurrence in the resection area, in regional lymph nodes, or in adjacent tissue occurs more often when the tumor is located distally in the colon. Most of these recurrences (±75%) take place 2–3 years after surgery [16, 17]. The highest incidence of local recurrence occurs in the case of a tumor located in the lower rectum, probably resulting from close proximity to other organs and tissues and due also to the limited possibility for radical excision [17–20]. The high recurrence rate is caused by residual tumor cells of the primary tumor, or the tumor in regional lymph nodes. Depth of tumor invasion through the bowel wall and in surrounding tissues appears to be a major risk factor [14, 21–23]. Up to 90% of local failure has been described in the case of rectal cancer with extension through the bowel wall.

Theoretically, tumor cells from other metastases may also home in the primary tumor bed but this is very difficult to evaluate. Furthermore, intraoperative tumor spillage resulting in implantation and outgrowth of tumor cells is also considered an important cause for local recurrence. The spilled tumor cells may settle in places [22, 24, 25] with low resistance such as the suture line, then grow out and lead to recurrence. The intact mucosa appears rather resistant to implantation [26]. This intraoperative contamination of the surgical field probably plays an important role and may be caused by spillage from an accidentally opened bowel lumen or from contamination of instruments or sutures.

Local recurrence can occur separately from distant metastases. The incidence of local failure alone without evidence for dissemination varies according to the literature from +20% to 60% [13–15, 17, 18, 21, 27–31]. Resection of local recurrences should play an important role in the therapeutic arsenal for colon cancer for local recurrences that occur separately from systemic dissemination. Moreover, prevention of local recurrence should be a major effort in primary surgery for colorectal cancer.

Prevention of Local Recurrence

Prevention depends then on optimal care during the surgical procedure, which means a radical form of surgery and avoidance of spilling tumor cells from the bowel lumen and the tumor itself. Radical surgery should minimize the chance of suture line or bowel wall recurrence and of recurrence in intramesenteric lymph nodes or surrounding tissue. The extent of resection depends on the expected spread of tumor in and close to the bowel wall and mesenteric lymph nodes. It has been shown in many clinical studies that intramural spread in the bowel wall usually does not exceed 2 cm [32–37]. As the length of bowel wall resection is in fact determined by the extent of mesenteric resection, the problem of bowel wall margin is only relevant in low anterior resection, in which a 2-cm distal margin can be excepted, provided that histopathological study of the distal resection area during operation proves to be negative. Studies in which low anterior resections are compared to abdominoperineal resections do not show higher recurrence rates in the former group [38, 39]. Adequate resection of the intramesenteric lymph node area and surrounding tissue is important in the prevention of local recurrence. Lymphatic vessels of the colon wall drain in the subserous plexus and in the intramesenteric lymphatic system. The lymph drainage of the colon is intramesenteric in an upward direction along the vascular tree, passing 5 groups of lymph nodes. The first group consists of the epicolic lymph nodes and the last group in the mesentery is situated at the base of the main mesenteric artery. From here the drainage moves upward along the para-aortic and vena cava nodes. From the rectum the lymphatic flow moves upward along the superior hemorrhoidal vessels, but a lateral flow exists to the hypogastric lymph nodes in the last 7–10 cm of the rectum, and to the inguinal lymph nodes from the most distal part of the rectum.

Limited Versus Extended Resection

Adequate resection of involved lymph nodes is feasible by removing the mesenteric drainage area. The question is how large this area should be in width along the marginal arteries of bowel wall as well as in the cranial direction to the base of the mesenteric artery and even further along the aorta. For more distal lesions pelvic lymphadenectomy has also been performed [40–42]. Obviously, in the modern concept of surgical oncology, such extended resections of involved lymph node areas do not fit. Extensive lymph node involvement will, in most cases, imply systemic tumor dissemination. It has been shown that lymphaticovenous shunts do exist and tumor cells may pass from blood vessels to lymphatic vessels and vice versa [43, 44]. Involvement of all levels of lymph node groups indicates incurable disease, but can we establish the level of lymph node involvement that still enables us to execute curative resection? This question has prevailed since the beginning of this century [45, 46] and one should be able to consult a few well-conducted randomized trials for a solution. Since, however, this is not the case, retrospective studies have to provide some answers. A few studies have investigated the so-called extended resection. Limited versus extended lymphatic dissection most often implies ligation of the vascular pedicle at a low versus high level.