LIMITING THE RESECTABILITY IN LOCALLY ADVANCED PRIMARY OR RECURRENT CARCINOMA OF THE COLON

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ABSTRACT

PURPOSE: The terms of 'unresectable', 'inoperable' and 'incurable' cancer/patient are widely used but not clearly defined and thus subject to significant subjectivity. Where is the limit of 'resectability' of colorectal cancer - the criteria are variable and not precisely defined yet. Locally advanced lesion may vary from visible intimately adhered to the surrounding tissue, i.e. marginal, 'border' resectable tumour to one that directly macroscopically engages adjacent critical structures. This paper presents the experience of other foreign authors with their results in the determination of the tumour as resectable or unresectable as well as own clinical experience in this field.

MATERIAL AND METHODS: The study covered the patients with colorectal cancer who were operated in the Clinic of Surgery during a period of 9 years and retrospectively analyzed.

RESULTS: Out of a total of 1051 surgeries on the occasion of colorectal cancer, advanced disease constituted 28,6% or 301 patients. Of them, 52,5% were localized in different parts of the colon. Fifty-eight combined resections were performed as in 7 of them (recurrent tumours) R1 was accomplished, i.e. a non-radical result. A total of 117 cases were assessed intraoperatively as non-radical surgery and palliative procedures were performed such as resections (with or without restoration of the intestinal passage, but in the case of M1), bypass anastomoses, or simple interruption of the passage. .

CONCLUSION: Many of the world's leading surgical centres adopt the tactics of 'adequate aggressive behaviour' for locally advanced primary and recurrent colorectal cancer. In determining the reasonable balance between aggressive approach and the so-called meaningless 'surgical exorbitance' there is strive to adhere to the view that failure to achieve R0-resection planed in such an operation as well as leading performance or a combination of factors such as advanced age, severe co-morbidities, presence of complicated forms of colorectal cancer, urgent intervention and data of generalization of the malignant process undermine the performance of aggressive block removal of tumour formation. However, adequate pre- and intraoperative assessment and surgical experience should avoid 'exaggerated' intraoperative status of locally advanced tumour and passive determination as 'unresectable'.

Key words: *colon cancer, resectability, primary colon cancer, locally recurrent colon cancer, surgery*

INTRODUCTION

Cancer of the colon and rectum (colorectal cancer, CRC) is ranked second in prevalence rate. In men, it comes second after lung cancer, and in women it comes second after breast cancer. Ages between 50 and 70 years are most often affected, and it is slightly more frequent in males than in females. There is a steady trend of annual increase of incidence rate in

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Bulgaria of 18,6 per 100000 inhabitants in 1984 up to 26,7 per 100000 in 1993. According to the National Cancer Registry for 2009, the incidence rate of colon cancer in men is 40,4/100000 and 32,2/100000 in women. The distribution of cancer of the rectum and anus is 30,5/100000 in men and 19,7/100000 in women, respectively. Colon cancer mortality rates are 11,8/100000 in males and 7,0/100000 in females, while those of cancer of the rectum and anus are 10,2/100000 and 3,8/100000, respectively (1). CRC is often curable disease when localized only in the gut wall. Surgery is the primary manner of treatment and cure is achieved in approximately 50% of the patients. Relapse after surgery is a major problem and is often the ultimate cause of death.

Locally advanced primary and recurrent CRCs are surgical challenge due to clinical presumption of tumour involvement of other structures and organs. Anticipated need for extensive surgical resection, often with multivisceral en-bloc resection is crucial for preoperative surgical planning. As for the primary and the recurrent tumors, postoperative long-term survival is achievable, but only after complete R0-resection. The role of neoadjuvant and adjuvant therapy continues to be seen in this era of biological chemotherapies and multimodal treatment provides an opportunity for the technical realization of resection and improves long-term survival.

According to the prospective SEER (Surveillance, Epidemiology, and End Results) program data in the USA from 1992 to 2003, staging and survival of almost 36000 patients with rectal cancer and 110000 ones with colon cancer analysis presented at the annual meeting of the American Society for Clinical Oncology in Chicago (2008 ASCO Annual Meeting), among the patients with tumour at IIB stage which extends through the intestinal wall and infiltrates the surrounding structures, no metastases to lymph nodes (T4 N0 M0) there is a worse chance of survival than among those with tumour at III stage which remains in the intestinal wall, but spreads to the lymph nodes (T1-2 N1-2) (2). Recent studies confirm that T4 stage is an important independent prognostic factor for disease-free interval and overall survival (3). Based on this, AJCC Hindgut Taskforce (HTF) validates change staging as stage IIB is divided into two substages: IIB T4a tumours are passing through the outermost gut layer (visceral peritoneum) and IIC T4b, where the tumour directly infiltrates other organs or structures. Stage IIC has a significantly worse chance of survival than stage IIB, IIIA or IIIB. Furthermore, some tumours that have spread to more than three lymph nodes (N2) are less likely to lead to death in the next five years than it was previously suspected and should be reclassified as IIIA (4). This population-based analysis of the survival validates rectal pooled analysis data analysis (5) and determines the change of T1-2N2 cancer from IIIC to IIIA/IIIB and T4bN1 from IIIB to IIIC. It also supports splitting IIB in IIB (T4aN0) or IIC (T4bN0) and displacement of favourable TN2 categories IIIC to IIIA (T1N2a) or IIIB (T1N2b, T2N2a-b, T3N2a, T4aN2a). The results of the TN category involve complex biological interactions between the depth of the primary invasion and lymph nodal status (6).

The determination of the colon cancer as locally advanced stage of the disease is necessary in order to achieve practical and theoretical clarity concerning a considerable percentage of patients presenting for treatment to the surgeon. Some patients with colon cancer present with a different form and extent of locally advanced or recurrent primary tumour process, but in a stage of non-metastatic disease, which, despite the lack of generalization, it may be resected. Criteria of unresectability are variable and not clearly defined yet. Locally advanced tumours defined by some authors as such are visualized by endorectal ultrasound as T3/4 or N1 tumours, or ones that are clinically diagnosed through physical examination, but without any distant metastases (7,8). The American Joint Committee on Cancer staging schema classify them as T4 lesions (9).

An appropriate working definition of locally advanced CRC is that the final evaluation of the multidisciplinary team managing the patient presented by surgeons, pathologists, radiologists, medical oncologists, gastroenterologists and imaging diagnostic specialists is precise and standard single-organ resection could be made, no more likely to remain in the specimen of the surrounding tissue and spaces of microscopic or macroscopic residual disease detectable due to adherence or fixation of the tumour to the surrounding structures. Locally advanced lesion may vary from visible intimately adhered to the

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surrounding tissue, i.e. marginal, 'border' non-resectable tumour to one that directly macroscopically engages adjacent critical structures (e.g. main dishes, duodenum, pancreas, pelvic bones, lateral or anterior abdominal wall, other parts of the colon or small intestine or its mesentery, internal genitalia or organs of the urinary system, nerve plexuses, etc.). Usually, locally advanced cancer of the left colon may directly infiltrate the left kidney, spleen, abdomen, stomach and distal pancreas. Sigmoid cancer may invade into the bladder, ovaries, and uterus. Right-sided colon cancer can affect liver, pancreas, duodenum, and right kidney. A case of advanced right-sided colon cancer in engagement with the duodenum or pancreas, or both, is a dilemma for colorectal surgeons.

Preoperative imaging methods are often unable to provide accurate information about the duodenopancreatic invasion. Upper gastrointestinal endoscopy may fail to identify duodenal infiltration because tumour infiltration may be limited to the muscle layer without macroscopic invasion of duodenal lining. In this particular situation, intraoperative decision to perform pancreatoduodenectomy is difficult. Tumour mass is usually too big to adequately characterize the tumour boundaries. Patients with limited effect on the wall of the duodenum can be safely treated by partial resection and subsequent plastics, while for some larger parts of duodenal wall or pancreas pancreatoduodenectomy is required (10). Literature data indicate that most surrounding structures and organs are affected at primary site of the tumour in the sigmoid colon and rectum – in 66-89% of cases. Reasons are the high incidence of carcinoma localization in these areas, the mobility of sigma and close spatial proximity of the structures in the pelvis (10-13). Defining the locally advanced stage of the disease depends on a clinical assessment of resectability, pre-operatively or intraoperatively. In some cases, 'inoperable' tumour assessed as such in clinical or radiographic imaging studies may with subsequent intraoperative exploration be amenable to curative resection (8). 'Locally advanced' tumours represent 5-22% of all CRCs (14,15). The lack of local tumour control, especially in locally advanced CRC has disastrous consequences such as intestinal or urinary obstruction, bleeding from the lower gastrointestinal tract, morphological and functional disorders of the other surrounding organs, fistulizations and considerable pain. Successful eradication of locally advanced CRC would provide better survival and quality of life. Many researchers report in a number of cases the possibility of en-bloc resection (14,16-18) and some of them demonstrate significantly better long-term prognosis and actual survival.

Complete removal of the tumour by achieving a negative resection lines is critical to obtain long-term results in terms of survival and, generally, frequently requires multivisceral block resection. This needs focusing on clinicopathologic features associated with such co-morbidity and predictors of long-term survival in patients undergoing surgery for locally advanced and locally recurrent CRC, together with the established role of neoadjuvant or adjuvant chemotherapy and radiation. As highlighted, the benefits on survival and quality of life after multivisceral resections are often associated with markedly higher postoperative morbidity rate (11,19,20), however, because of improved surgical technique and experience, the complications gradually reach the level common in non-block resections (15,21).

In about 10% of colon carcinoma cases, tumour conglomerates affect adjacent structures. Histologically demonstrable permeation, however, is only in about 50% of these cases, with the remainder being caused by adhesion due to peritumoural inflammation. In both cases, a multivisceral resection in unit is necessary to remove all structures involved, as the goal is to achieve R0 resection taking into account the ways of the lymphatic drainage of all the bodies involved. The complete resection is a prerequisite for long-term survival. In the case of locally advanced colon cancer, the determination of the difference between the benign and malignant invasion adhesions is often not possible in the operating room. Since dissection of malignant fistula or infiltration and disruption of tumour integrity are associated with tumour dissemination and poor outcome due to early local recurrence and reduced survival, en-bloc resections of the affected structures are widely recommended. In most cases, this may require multiple organ resection, but safe treatment is possible only if it achieves R0-resection. If the organs involved in primary tumour conglomerate are intraoperatively separated, histological confirmation of true infiltration can intraoperatively be obtained, e.g. in case of carcinoma located in the right flexure involving pancreatic head before a decision is made to perform a combined pancreaticoduo-

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denectomy increasing the risk of locoregional recurrence or peritoneal carcinomatosis due to the generalization of tumour cells in the abdominal cavity, by about two times. The possibility of indeterminable or false-negative results by gefrire examination should not be underestimated. Therefore, multiorgan resection is undertaken only in cases when it can be avoided through the tumour mass and tumour cell scattering. Proper interpretation of the physical signs and symptoms of multivisceral involvement and appropriate use of preoperative imaging ensure that a multidisciplinary oncology team would make the correct decision in order to direct the surgeon to extended resection when necessary. Similarly, achievement of complete resection of locally recurrent CRC is essential for long-term survival. Dissection of the structures often challenges because of the deletion of anatomical plans following the previous operation, which represents a significant technical difficulty to multivisceral resection. Implanting radiopositive marker clips can be useful in mapping the areas of dissection, when postoperative radiotherapy is intended.

The majority of patients with locally advanced tumours present with symptoms such as back or lumbar pain, nausea or vomiting indicating some degree of obstruction or frank haematuria. Frequently, symptoms target localization of disease, e.g. bladder invasion is associated with dysuria and haematuria and in case of pathological fistula there is gas in the bladder through the urethra and in micturition as well as leakage of urine through the anus. As might be expected, the most frequently implicated tumour pathologies are anatomically similar to the primary lesion: cecum and sigmoid carcinomas are usually associated with the ovaries, fallopian tubes, uterus, and small intestine, whereas hepatic flexure, or transversal colon-lienal flexure more frequently infiltrate gallbladder, duodenum, stomach, pancreas, and spleen. The abdominal wall is more likely to be affected by intraperitoneal parts of the colon, and the retroperitoneum is more likely to be infiltrated by the lesion located in the two folds or ascending and descending colon.

Locally advanced lesions generally are larger and often palpabale on physical examination. Colonoscopy can reveal, to varying degrees, annular stenosing or obstructing constriction bands, usually bleeding easily when touched. Image data from computed tomography (CT), magnet resonance imaging (MRI), and positron-emission tomography (PET)-CT often show suspicion of infiltration or presence of subtle malignant fistula. They could not, however, distinguish between peritumoural inflamma-

Table 1. Role of imaging examinations in CRC

Purpose	Accuracy		
	CT	MRI	PET
Initial preoperative staging	48-77%		
T-staging of rectal cancer	77%	85%	
Detection of liver metastases	73-82%*	82-97%*	77-92%
N-staging	23-73%	85%	
Imaging vascular anatomy for planning resection (recommended)			
Staging of recurrent disease	sensitivity of 46-69% specificity of 96%		sensitivity of 79-93% specificity of 96%

**If severe steatosis is present, accuracy for detecting liver metastases drops to 48% by CT and to 70% by MRI*

**PET does not play any role in initial staging unless extrahepatic disease is suspected or results from other imaging modalities are equivocal.*

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tion by direct tumour infiltration in the absence of a 100% 'sensitivity' and 'specificity' of these diagnostic methods. Ultimately, the surgeon must intraoperatively decide whether it is necessary and whether it is technically possible to perform combined resection.

Table 1 compares the diagnostic capabilities of these imaging methods in patients with CRC (24).

Lymph node size of 3-6 mm is considered intermediate (undefined); >6 mm - suspected; >8 mm -malignant. 3T MRI is more accurate than 1,5T image. Enhanced diffusion MRI technique (diffusion-weighted MR imaging, DWI) possesses the largest diagnostic capabilities compared to other modalities in determining the N-status (24).

Prognosis of locally advanced tumours is not poor when they are fully resected in tight. A more difficult situation arises when the combined resection involves higher risk procedures such as partial duodenectomy and/or duodenohemipancreatectomy. Eight cases of T4 tumour formations of the right colon requiring pancreatic or duodenal resection were reported (25). Either a right colectomy to block duodenectomy (n=4), or pancreatoduodenectomy (n=4) were performed to ensure R0 resection. There were only two non-severe complications and no deaths. Six patients remained 'free' of the disease at an average follow-up of 26 months, and one - during a 'disease-free' period of 84 months. In another study (11), 12 patients underwent partial block duodenectomy (n=5) or pancreatduodenectomy (n=7) for resection of colonic cancer. Eight patients were described as 'free' of the disease at an average of 42 months follow-up. A 'disease-free survival' for a period of 10 to 113 months was reported elsewhere (26). These rates provide evidence in support of the aggressive behaviour in resection of adjacent organs, including the pancreas, for locally advanced colon cancer provided that it can be performed with an acceptable level of morbidity and mortality rates. When a surgeon is not willing to take an extended resection it is better the patient being taken to a centre with sufficient experience in multivisceral resections than being allowed to conduct an incomplete (R1 or R2) resection.

Urgency of the transaction often triggered by complications typical for locally advanced CRC has been identified as an independent risk factor for poor outcome in terms of long-term survival (23). The possibility of conservative management of specific complications when it is real and not associated with increased risk for the patient would allow conversion of the emergency procedure into elective surgery after assessment by a multidisciplinary team and with favourable conditions for the implementation of complete mesocolic excision (CME) with a radical operation.

Primary anastomosis in case of tumour obstruction of locally advanced colon cancer in left-sided positioning can be performed only when the ileus dilation is in an initial stage, the walls of the proximal bowel are not overstretched and lack any evidence of bacterial translocation and peritonitis, as well as risk profile such as age, homeostasis abnormalities and co-morbidities is favourable. Obstruction in advanced and high risk cases should be managed by discontinuity operation of Hartmann. According to various authors, protective proximal stoma, primary resection and anastomosis do not provide any advantage. Data from the multicentre study (27) present an assessment of the status of the surgical treatment of malignant obstruction of locally advanced cancer of the left colon in Germany and compare different operational approaches in the emergency treatment of this complication, especially diversionary operations (Hartmann procedure) and primary anastomosis. Among 15911 patients with cancer of the left colon reported between 2000 and 2004, a total of 743 patients underwent emergency surgery for malignant obstruction caused by locally advanced cancer, who had undergone radical resection. These patients were compared with respect to their risk profile and postoperative results. In 57,9% (n=430) a single-step radical surgery (group I) was done, in 11,7% (n=87) - a primary resection anastomosis with outlet protecting stoma (group II), and in 30,4% (n=226) - a diversionary Hartmann procedure (group III). In group III, most patients were male, with overweight, polymorbidity and more advanced tumours. Hospital morbidity and mortality (e. g., overall hospital mortality of 7,7%; n=57) did not differ significantly between the three groups. Preventive placement of temporary protective stoma did not influence on the rank of anastomotic insufficiency (group I, 7% and group II, 8,0%).

Local recurrence after primary CRC treatment, per se, is also variable concept concerning the acceptance by surgeons. It would appear as:

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- local recurrence with the same histological characteristics or negative grading progressed towards low differentiation, the site of anastomosis in previous comprehensive surgery - resection with subsequent reconstructive stage anastomosis, or

- locoregional recurrence - in the surrounding of the primary tumour removed - in incomplete R1 resection or inadequate removal of regional and lymph vessels or lymph-node pool, extensive perineural invasion, not covered in the removed specimen, iatrogenically implanted tumour bed in tumour cells (however, no No-Touch rule Turnbull is responsible for both locoregional recurrence and generalized organ metastasis through blood and lymph channels, and implantation metastasis throughout the operative field and surgical wound) (22).

Approximately 40% of the patients with resected colon cancer develop recurrence and most of them exhibit initially distant spread of the disease. Locoregional recurrence is much less common and accounts for 10% to 20% of recurrent cases. Cause of local recurrence include incomplete resection of transmural or lymphatic dissemination of the disease, integrity of the tumour or implantation of tumour cells. Surgery remains the primary treatment method, but it is clear that (R0)-resection can achieve long-term survival only.

The largest series of sweeping operation of locoregional recurrences were reported from Memorial Sloan-Kettering Cancer Center (MSKCC) (28) and Mayo Clinic (29). MSKCC series describe 100 patients and Mayo Clinic series report 73 patients. In two series of patients who have initially undergone a particular type of primary resection of tumour-bearing part of the casing, and subsequently developed locoregional recurrence, respectively, laparotomy was done as an intended curative resection of recurrences. In MSKCC series, the main reasons that led to relapse are generally advanced tumours extending through the intestinal wall, T3 or T4 were present in 85%, obstructing colon tumours were found in 11% and tumour perforation in 13%. Both studies confirmed that the majority of the primary tumours were located distally to the left flexure. Metastases in the lymph nodes were noted only in 50% of patients in the MSKCC study and in 60% in Mayo Clinic one, which indicated that the mechanism for the development of locoregional recurrence usually involved incomplete primary resection of the tumour in widespread area. This hypothesis is supported by the large-scale retrospective series of patients with colon cancer in which locoregional recurrences are envisaged on the basis of nodal status of primary disease.

Subgroup of patients with stage II CRC is considered to be that with the highest degree of risk of relapse/metastatic disease on the basis of: 1) tumour obstruction/perforation, 2) <10 removed lymph nodes at surgery, 3) T4 lesions and 4) invasion of the lymphatics or blood vessels (30). Their prediction is considered comparable to that of patients with stage III (T1-4 N + M0) and, therefore, it is highly recommended to use them with adjuvant chemotherapy. MSKCC and Mayo Clinic are similar concerning the classification of disease recurrences by dividing them into four groups. They are perianastomotic (intramural disease), mesenteric (involvement of regional lymph nodes), retroperitoneal (implantation metastasis, distant nodal disease or transmural residual disease), and peritoneal (implantation metastasis). When a relapse is detected, there is often a significant overlap and uncertainties in these categories. However, this scheme has its prognostic significance (28,31). In MSKCC series perianastomotic unilateral recurrences prevail (in 36%) followed by peritoneal (in 16%), mesenteric (in 15%), and retroperitoneal (in 12% of the cases). It is not surprising that two synchronous recurrent formations are noted in 21% of cases, with the most common combination involving anastomosis and regional peritoneum. Interestingly, the localization of the relapse associated with the clinicopathologic characteristics as the left-hand primary tumour is more commonly associated with recurrent anastomosis and the clinical obstruction is associated with peritoneal dissemination of disease relapse.

Mayo Clinic series attempt to delineate more precisely the different types of lymph node location on the form of relapse. Although some cases of relapse are due to inadequate resection with mesenteric lymph node dissection, most recurrent sites of lymph nodes are in regions which are not included in the

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standard oncological resections of colon (t.e. aortic, celiac, and iliac lymph group).

Surgical results in locally recurrent colon cancer

In the MSKCC series of 100 patients undergoing surgery with curative purpose, 56 patients underwent complete resection en-bloc. Thirty patients underwent incomplete resection as 11 were with microscopic and 19 with macroscopic residual disease. Fourteen patients were considered unresectable at exploration. Complete resection in 41 patients consisted in en-bloc removal of the tumour with surrounding organs or structures, usually in the abdominal wall, ureter, kidney, stomach, uterus, and pancreas. Nine patients underwent resection of multiple organs. Twenty-six patients had distant synchronous condition judged resectable. Overall, 21 of these patients underwent complete remote metastasectomy. The average hospital stay was 9 days, operative mortality rate was 1%, and perioperative morbidity rate was 24%. The incidence was highest (36%) among 14 patients considered inoperable during operation. Thirty-one patients received extracorporeal and/or intraoperative radiation therapy as part of a treatment plan.

The result of the operation in cases with curative locoregional recurrence is closely related to 'completeness' of the resection. In the MSKCC series, statistical 5-year survival for the entire cohort was 35%, with a median survival of 30 months. In 56 patients with complete (R0) resection, 5-year survival is 58% and the median survival time was 66 months. Incomplete resection, or as a result of microscopic (R1) or macroscopic (R2) residual disease is associated with significantly worse results. The median survival for patients with R1 (n=11) and R2 (n=19) resection is 25 and 23 months, respectively. There was no 5-year survival in cohorts of patients who underwent incomplete resection. In this series, 14 patients with laparotomy deemed unresectable and their median survival was less than 12 months.

In addition to the completeness of resection, MSKCC series describe several factors that predict outcome after curative operation, including the number of recurrences, location, pre- and postoperative CEA values, age, details of distant disease and stage of the primary tumour. Classification scheme for local recurrences also determines the predicted outcome. Patients with more than one location on locoregional recurrence and those with evidence of mesenteric recurrence have poorer results than with anastomosis, retroperitoneal or peritoneal relapses. The presence of synchronous distant metastases has an adverse outcome, too. However, 12% of patients with distant spread and local recurrence are living longer than 5 years after curative resection, indicating that the presence of the synchronous solitary distant metastasis is not a contraindication for curative operation provided that it is technically possible to remove the metastasis in tight. Time to recurrence is not a significant predictor of the outcome, which is somewhat surprising, since prolonged disease-free interval assumes more favourable tumor biology (32). This can provide impartial data that is inherent in retrospective studies (33). No doubt that the degree of 'enlargement' of resection and number of adjacent organs removed during surgery does not affect the result as long as R0 resection is achieved.

Mayo Clinic series included 73 patients who underwent surgical exploration for locoregional recurrence. Complete resection was achieved in 52% of them. Incomplete resection such as macroscopic and microscopic residual disease was done in 26% and 22% of the cases, respectively. On average, 51% of patients had complications, 70% were small and 30% severe, including one patient with perioperative death. All the patients received either external beam radiation and/or intraoperative radiation in the course of their treatment. For the entire cohort, statistical 5-year survival was 25% and median survival was 33 months (reported from the time of diagnosis of recurrence). Complete (R0) resection was performed in 38 patients (52%) and was associated with a significant improvement of the 5-year survival in 37% of the cases. Thirty-five patients underwent incomplete resection - 19 with microscopic (R1) and 16 with macroscopic (R2) residual disease. There was no statistically significant difference in the cohort of patients resected incompletely, with 25% of 5-year survival rate and lack of a 5-year survival rate in the R2 group. These results highlighted the well-described link between quality of resection (R0, R1, and R2) and output. Long-term survival was rare, if it existed at all, in patients with partial resection. It turned out that all the residual tumour areas - macroscopic and microscopic, negatively affected the results. The challenge for the clinicians is to determine which patients may be evaluated to un-

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dergo complete surgical resection and thus to prevent incomplete resection, which simply slows the application of other, non-surgical treatments.

MSKCC series was large enough to identify factors associated with complete (R0) resection of locoregional recurrence. Among the patients with a single location of the disease, perianastomotic form (unlike the mesenteric, retroperitoneal or peritoneal) of recurrence, low preoperative CEA and absence of distant metastases were more likely to be the cause of long 'disease-free' interval after a successful operation. Although not absolute, these factors can be identified on the preoperative tests, which would help the evaluation of patients for surgical success. In the patients with peritoneal disease and nodal/mesenteric form of relapse in more than one location, elevated CEA and synchronous distant metastatic disease hamper to achieve complete curative resection and in such cases, preference is given to neoadjuvant therapy prior to surgical resection.

MATERIAL AND METHODS

Retrospective analysis of patients with proven CRC surgery at the Clinic of Surgery, Alexandrovska University Hospital of Sofia Ltd for the previous 9 years was carried out. Documentary evidence from patient's history, operative reports, operational logs were used. Data from the Clinical Centre of Anatomy at the same university hospital where the histological examinations and pathologic staging were performed were analyzed. Protocols from specialized oncology hospital committees with final staging of patients and decisions of oncology committee were examined. Statistical data processing was performed with IBM SPSS software.

RESULTS

The operational activity was on an average of 1100 operations per year. During the 9-year period, a total of 1051 surgical patients with histologically verified CRC were treated. Cases of advanced malignancy accounted for 28m6% or 301 patients. The average patient's age was 67,4 years. Of them, 68% were males and 32% females. In 552 operated patients (52,5%), cancer was located in different parts of the colon. There were 175 patients with locally advanced colon cancer, 32 recurrent and 143 - primary. In 58 patients, complete combined resection of locally advanced tumour block infiltrating the surrounding structures and organs was performed. In 7 of them, the final histological results showed failure to achieve radical excision of infiltrative surrounding tissues (R1). They were recurrent tumours with massive infiltration of large areas. Some 117 palliative (non-radical) interventions were performed - in 90 patients, inability of radical surgery was caused by pre- and intraoperative detection of a generalized cancer process, bilobar unresectable multiple liver metastases and/or diffuse carcinosis of peritoneum. In the remaining 27 patients, the decision about inability of radical resection of carcinoma was caused by the general extraorgan infiltration of surrounding structures - in 18 patients with intraoperative assessment of the lack of sufficient probability of achieving R0-resection, while in the remaining 9 ones the reason was urgency of intervention due to serious complications (mostly obstruction or perforation - tumour or diastasis with diffuse peritonitis or total one) and/or advanced age with severe decompensated comorbid background. Although in 34 of these 117 non-radical surgical cases resection of the primary tumour was performed (in the technical possibility and preserved functional status of other organ systems), the presence of irremovable distant metastases characterized the operation as a palliative.

DISCUSSION

Many eminent surgical centres promote the idea of 'adequate aggressive behaviour' for locally advanced primary and recurrent CRC (34). However, this inevitably requires individualized and comprehensive assessment of each case based on the use of the full resources of diagnostic methods for preoperative staging, as well as a broad discussion of the results of a multidisciplinary team before undertaking the operation. Our vision largely overlaps with the opinion of most of these authors about the circumstances that determine the decision for unresectability of locally advanced CRC. In our practice, we performed a combined removal of colon tumour and duodenopancreatic resection of the infiltrated sections of the duodenum or the head of the pancreas. There are benefits of long-term survival and disease-free interval/intra- and postoperative complications. In contrast to other studies (11,25,26), the small number of our patients operated on and followed did not warrant any representativeness of the

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sample. Along with assessing the status of all vital organs and systems, evidence or lack of generalization of the process, presence of complicated forms of CRC and emergency or planned manner of operation, macroscopic features of malignancy as assessed with intraoperative exploration prove decisive for their assessment of resectability, which depends very much on the experience of the operating surgeon responsible for the patient. In 27 of our patients, factors such as extent of the estimated gross infiltration engagement, missing critical structures and/or worsening performance-status because of severe comorbidities favouur the decision that ends 'aggression' per se would be unnecessary and even harmful to patient's short-term and long-term prognosis.

Opinion of all authors, including ours, to consolidate the idea that failure to achieve R0-resection undermines the performance of aggressively block removal of tumour formation, while simultaneously, pre- or metachronous removal of oligometastases in the liver remains controversial. In 7 of the locally advanced recurrent tumours, block resection with intraoperative macroscopic presumption of radical surgery were committed, but the final histological results showed microscopic infiltration in some areas of the excised infiltration. Since it is a massive infiltration at the 'edge' of technical ability and poor general condition of the patients, some of them elderly, no re-Redo surgery could be reached to achieve histological, i.e. real radicality. All the authors emphasize the adequate consensus, called 'team' preoperative approach. In our practice, unfortunately, is not perceived by the Cancer Committee to report and treat patients in the phase before any operation. Especially in recent years, a limitation and complex use of the full range of highly specialized and high-technological diagnostic imaging methods are reasons of subjective and objective nature as the economic reasons are leading. Most authors adopt the view concerning the indications of combined preoperative chemotherapy in order to increase the possibility of planning the operation as 'potentially curative'.

Preparation is imperative to validate a standardized strategy for management of patients with advanced (locally or generalization) CRC, delineating and clearer criteria for resectability and, consequently, unresectability of the primary or recurrent tumour, and for the prospects of neoadjuvant therapy.

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