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# The management of peritoneal surface malignancy of colorectal cancer origin

**Abstract** Colorectal carcinomas are predominantly spread malignancies. Peritoneal carcinomatosis frequently associates colorectal carcinomas. The tumour grade, the completeness of cytoreduction, the tumour volume, the presence of distant metastases, prior surgery score and the extent of peritoneal implantations are prognostic clinical features of survival. The management of colorectal cancer with peritoneal carcinomatosis is possible by resection of tumour, cytoreduction and intraperitoneal chemotherapy. $T_3$ and $T_4$ colorectal tumours are at risk of developing locoregional recurrence and may be treated by intraperitoneal chemotherapy. Early postoperative intraperitoneal chemotherapy has been used in 40 patients with $T_3$ and $T_4$ tumours, with 15% hospital mortality, and 32.5% morbidity. The overall 3-year survival rate was over 80% and only 15% distant metastases were recorded.

**Key words** Colorectal cancer • Peritoneal carcinosis

## Introduction

Colorectal carcinomas are associated with peritoneal carcinomatosis in 10–15% of the cases at the time of initial diagnosis and at the time of recurrence in 58% of the cases. Colorectal cancer is a predominantly spread malignancy, as is every other intracealomic tumour [1–4]. Peritoneal carcinomatosis may occur either preoperatively spontaneously or intraoperatively iatrogenically. The preoperative development of peritoneal carcinomatosis may occur either from high grade tumours with random proximal distribution or from low grade tumours as a redistributed malignancy [5]. The intraoperative development of peritoneal carcinomatosis occurs particularly when resection is performed in narrow margins like the pelvis. During resection, from traumatised interstitial tissues, severed lymphatic channels or venous blood loss, spilled cancer emboli are attracted by the neighbouring traumatised peritoneal folds and are entrapped by blood clots. During wound healing by fibrin deposition, by the accumulation of inflammatory cells, and the stimulation of growth factors cancer emboli are promoted to macroscopically visible tumours of recurrence in approximately 2–3 years following initial surgery [5].

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## Clinical prognostic factors of survival in colorectal cancer with peritoneal carcinomatosis

A number of clinical factors prognostic of survival have been identified. The tumour grade is one of the most important factors once it has been demonstrated that patients with low grade tumours have significantly increased survival compared to those with high grade tumours. It has also been demonstrated that patients undergoing complete cytoreduction have significantly increased survival compared to those undergoing incomplete cytoreduction [6]. Cytoreductive surgery is assessed by the completeness of cytoreduction score after surgery indicated by four distinct operations. CC-0 is the operation leaving behind no macroscopically visible tumour. CC-1 is the operation leaving behind macroscopically tumour less than 2.5 mm in its largest diameter. CC-2 is the operation leaving behind macroscopically visible tumour between 2.5 mm and 2.5 cm, and CC-3 is the operation with residual tumour >2.5 cm. Complete cytoreductive surgery is considered only a CC-0 operation for high grade tumours but for low grade tumours CC-0 and CC-1 operations are considered complete cytoreductions [7]. The presence of distant and non-resectable metastases is an unfavourable prognostic factor of survival as is the presence of large volume implantations. Prior surgery score (PSS) has been demonstrated to be another important factor of survival. PSS is a number indicating the number of abdominopelvic regions that surgery has been performed for cancer in the past. The greater the number, the lesser the survival is. In addition, the extent and distribution of peritoneal carcinomatosis is another prognostic factor of survival. The extent of carcinomatosis is assessed in detail by the use of peritoneal cancer index (PCI). PCI is a number indicating the summation of the lesion size in each one the 13 different abdominopelvic regions that the abdominal cavity is separated into [6] (Fig. 1). The more extensive the peritoneal seeding is, the less the survival is.

## Surgery for peritoneal carcinomatosis of colorectal cancer origin

The most important step in the management of colorectal carcinomas with peritoneal seeding is cytoreductive surgery that is possible by peritonectomy procedures. There are 6 different types of peritonectomy procedures: (a) greater omentectomy combined with splenectomy, (b) right subdiaphragmatic peritonectomy, (c) left subdiaphragmatic peritonectomy, (d) pelvic peritonectomy combined with en bloc resection of the sigmoid colon and/or the upper rectum and the internal female genitalia, (e) cholecystectomy combined with resection of the omental bursa and (f) lesser omentectomy [7].

## Adjuvant therapy for peritoneal carcinomatosis of colorectal cancer origin

Even if a complete cytoreduction has been performed and no macroscopically visible tumour has been left behind, microscopic foci may have been left in the abdominal cavity. The eradication of microscopic foci is not possible by systemic adjuvant chemotherapy. Intraperitoneal chemotherapy gives high response rates within the abdomen because the peritoneal–plasma barrier provides dose-intensive therapy [8].

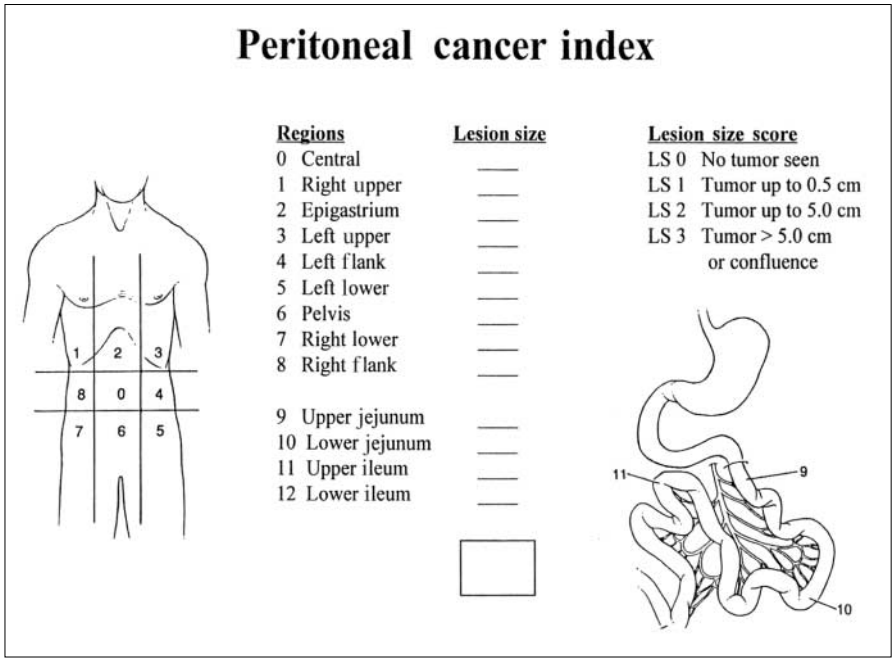


**Fig. 1** The assessment of the extent and distribution of peritoneal malignancy

It has been demonstrated by high performance liquid chromatography studies that the exposure of peritoneal surfaces to pharmacologically active molecules can be increased considerably by intraperitoneal administration once high-molecular-weight substances are confined to the abdominal cavity for long [9]. Intraperitoneal chemotherapy may be used either in the early postoperative period under normothermia (the first 5 postoperative days) or intraoperatively combined with heat [7]. It is well documented that heat increases drug penetration into tissues, has an antitumour effect by itself and increases the cytotoxicity of selected chemotherapeutic agents. If intraoperative chemotherapy is used when the abdomen is exposed, the surgeon's hand may uniformly distribute heat and cytostatic drugs to all surfaces of the abdomen and pelvis. In this case renal toxicities of chemotherapy can be avoided by careful monitoring of urine output. The time that lapses during heated chemotherapy perfusion allows a normalisation of many physiologic parameters (core temperature, blood clotting, haemodynamics etc.) [7].

## Preliminary results with the use of early postoperative intraperitoneal chemotherapy (EPIC) in $T_3$ and $T_4$ colorectal tumours

The use of early postoperative intraperitoneal chemotherapy has been recommended in an adjuvant setting for prevention of peritoneal carcinomatosis [7]. The method has been used since 1999 in 40 patients with $T_3$ and $T_4$ colorectal tumours. The selected patients (a) were older than 18 years of age, (b) were able to tolerate major surgery, (c) had stage II or III carcinoma, (d) had normal renal function (urea blood <50 mg/dl, creatinine <2 mg/dl), (e) had normal liver function and (f) had acceptable physical status (Karnofsky performance status >50%). Patients with (a) pregnancy, (b) prior malignancy at risk of recurrence (except for basal cell carcinoma and *in situ* cervix carcinoma), (c) presence of distant metastases and (d) evidence of diffuse peritonitis, were excluded. The morbidity rate was high (32.5%) (Table 1).

**Table 1** Morbidity of 40 patients with colorectal carcinomas receiving EPIC

| Complication | Patients, n | % |
|---|---|---|
| Cerebrovascular | 1 | 2.5 |
| Cardiovascular | 1 | 2.5 |
| Anastomotic failure | 4 | 10 |
| ARDS | 1 | 2.5 |
| Systemic sepsis | 2 | 5 |
| Diffuse peritonitis | 2 | 5 |
| Intra-abdominal abscess | 1 | 2.5 |
| Pancreatitis | 1 | 2.5 |

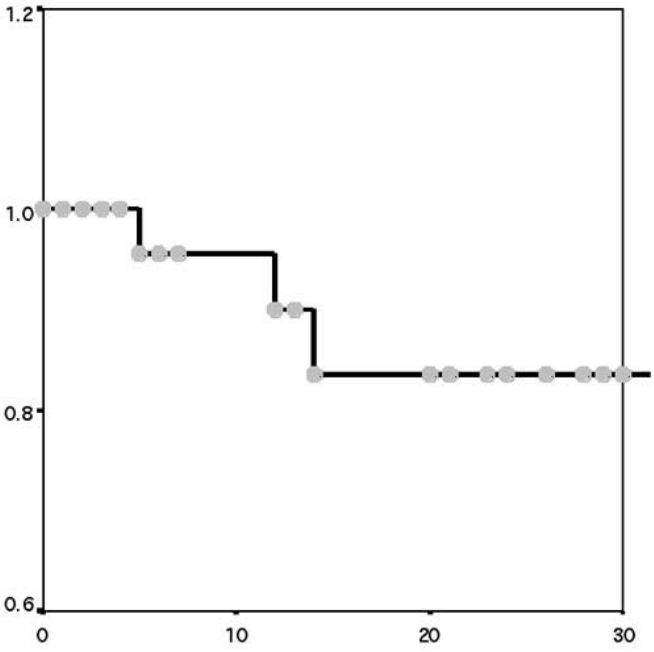


**Fig. 2** Three-year survival of 40 patients with colorectal carcinomas

Hospital mortality was 15% (6 patients) and by regular follow-up recurrence was recorded in 6 patients (15%). No locoregional recurrence was recorded. The 3-year survival rate was over 80% (Fig. 2).

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