Preoperative Assessment of Cancer Patients with Peritoneal Metastases for Complete Cytoreduction

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Abstract The purpose of this manuscript is to critically evaluate the preoperative assessments of peritoneal metastases described to date. Recommendations regarding use of current modalities and an assessment of their reliability will be made.

Keywords CT · MRI · PET · SPDSS · Concerning radiologic features · Peritoneal metastases normograms · Signet ring cells

Introduction

Progress in the management of peritoneal metastases from gastrointestinal and gynecologic malignancy has continued over the last three decades. Cytoreductive surgery (CRS) with peritonectomy procedures and visceral resections have become well defined and are currently completed with minimal morbidity and mortality [1, 2]. The second component of peritoneal metastases treatment is hyperthermic perioperative chemotherapy (HIPEC). This has progressed but to this point in time standards of care have not been formulated. Currently, there is not a consensus regarding an optimal HIPEC with or without early postoperative intraperitoneal chemotherapy (EPIC) but steady progress has occurred [3]. Also, a reliable group of prognostic indicators including histopathology, prior surgical score (PSS), peritoneal cancer index (PCI), and completeness of cytoreduction score (CC score) have been validated in peritoneal metastases from both gastrointestinal

and ovarian cancer [4]. There is one extremely important aspect of peritoneal metastases management that has lagged far behind the others. That is accurate preoperative assessment of the extent and distribution of the peritoneal surface malignancy. This accurate assessment prior to the abdominal exploration would be of great benefit. It would reduce the number of open and close procedures in patients having CRS plus HIPEC. Accurate knowledge regarding extent and distribution of peritoneal metastases (preoperative PCI) would provide crucial information to the surgeon and to the patient regarding the resection required for complete CRS and the likelihood of long-term benefit. Finally, accurate assessments would allow a stratification of patients so that a comparison between institutions of results of treatment is possible.

The purpose of this manuscript is to critically evaluate the preoperative assessments of peritoneal metastases described to date. Recommendations regarding use of current modalities and an assessment of their reliability will be made.

Histopathology Including Lymph Node Status

The histopathology of a gastrointestinal cancer has almost always been determined prior to an intervention using CRS and HIPEC to treat peritoneal metastases. Histopathology may be of great value in the preoperative evaluation of patients. For appendiceal epithelial neoplasms, the peritoneal metastases may be determined to be disseminated peritoneal adenomucinosis (DPAM), peritoneal mucinous carcinoma (PMCA), or peritoneal mucinous carcinoma with signet ring morphology (PMCA-S). Figure 1 shows the marked difference in survival of DPAM and PMCA [5]. In this assessment PMCA includes the PMCS-S histologies. In this same group of PMCA patients, Ihemelandu and Sugarbaker identified

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Fig. 1 Survival of patients with mucinous appendiceal neoplasms by histopathology. The graph includes all patients. The blue line ($N = 455$) indicates patients with adenomucinosi. The red line ($N = 492$) indicates patients with mucinous adenocarcinoma and includes patients with intermediate-type histology. (From reference 5 with permission)

patients who had signet ring or adenocarcinoid morphology. In the 80 appendiceal peritoneal metastases patients with signet ring morphology, median survival was 18.9 months as compared to 45.4 months for 361 PMCA patients in the absence of any signet ring cells. Median survival for 53 patients with adenocarcinoid morphology was 26.8 months ($p = 0.000$) [6].

For colon cancer, signet ring peritoneal metastases also indicates a poor outcome with peritoneal metastases treated with CRS and HIPEC. Verwaal and colleagues reported 15 patients with signet ring cells had a median survival of 13.0 months as compared to 86 patients without signet ring cells identified in peritoneal metastases had a survival of 21.4 months ($p = 0.008$). These authors recommended that signet ring cells in peritoneal metastases are a relative contraindication to the use of CRS and HIPEC to treat peritoneal metastases in colon cancer patients [7]. Also, it is well established that signet ring cells carry a poor prognosis in patients with gastric cancer. In treating gastric cancer peritoneal metastases, signet ring cells indicate a near low likelihood for long-term survival for patients having CRS and HIPEC [8].

Regional lymph node status of the primary appendiceal cancer has prognostic implications. In 273 PMCA patients, 47 were determined to have lymph nodes positive in the mesoappendix or in the ileocolic lymph node group. The patients treated with CRS and HIPEC with positive lymph nodes had a worse prognosis (Fig. 2). However, the data on lymph node positive appendiceal metastases patients shows that the prognosis is sufficiently favorable to recommend CRS and HIPEC if complete cytoreduction is considered probable [5].

Elias et al. in a multivariate analysis of 523 patients with colorectal cancer peritoneal metastases showed that positive

Fig. 2 Survival of patients with peritoneal mucinous carcinoma by the absence of disease in regional lymph nodes (blue line, $n = 225$) vs. its presence (red line, $n = 47$). (From reference 5 with permission)

regional lymph nodes indicated a reduced prognosis ($p = 0.02$) [9]. In colon cancer patients treated in Washington, DC with CRS and HIPEC for peritoneal metastases, 14 had no regional lymph node metastases and 53 had positive lymph nodes identified. Figure 3 shows the difference in survival by lymph node status ($p = 0.03$). Clearly, negative lymph nodes indicate an improved prognosis when peritoneal metastases are treated by CRS and HIPEC [10].

Prior Surgical Score (PSS)

In a large majority of patients, if peritoneal metastases are treated with CRS and HIPEC, there are surgical procedures performed prior to the definitive procedure. The extent of prior surgery can be quantitated using an assessment called the prior surgical score (PSS) shown in Fig. 4. The PSS will

Fig. 3 Kaplan-Meier survival curves for patients with lymph node negative (dashed line, $n = 14$) or lymph node positive (solid line, $n = 53$). Log-rank $p = 0.03$. In three patients, information about lymph node status was unavailable. (From reference 10 with permission)

Fig. 4 Abdominopelvic regions used to determine the prior surgical score (PSS). Two transverse planes and two sagittal planes are used to divide the abdomen into 9 abdominopelvic regions (AR-0 through AR-8). The upper transverse plane is located at the lowest aspect of the costal margin. The lower transverse plane is placed at the anterior superior iliac spine. The sagittal planes divide the abdomen into three equal sectors. These lines define 9 regions, which are numbered in a clockwise direction with 0 at the umbilicus and 1 defining the space beneath the right hemidiaphragm. (From reference 11 with permission)

Determination of prior surgical score

Prior Surgical Score

- 0 Central
- 1 Right upper
- 2 Epigastrium
- 3 Left upper
- 4 Left flank
- 5 Left lower
- 6 Pelvis
- 7 Right lower
- 8 Right flank

Prior Surgical Score	Description
PSS-0 (none)	Biopsy only
PSS-1 (minimal)	Exploration laparotomy, 1 region
PSS-2 (moderate)	Exploration laparotomy with resections, 2 to 5 regions
PSS-3 (extensive)	Extensive prior cytoreduction, >5 regions

estimate the adhesive process that the surgeon will encounter during the reoperative event. More importantly it is an estimate of the extent of tumor cell entrapment that has occurred and will need to be resected as part of a complete CRS [12]. If only a biopsy was performed, the PSS is zero. If there was a prior exploratory laparotomy and a single abdominopelvic region was dissected, the PSS is one. If two to five regions are previously dissected, the PSS is two. If there was a prior attempt at cytoreduction and more than five abdominopelvic regions were involved in the surgical procedure, the PSS is three [11].

For appendiceal mucinous neoplasms with DPAM histology, PSS had a profound effect on survival in patients treated with CRS and HIPEC. Ten-year survival with PSS 0–2 was 75 % as compared to 55 % with PSS of 3 ($p < 0.0001$). For PMCA, the PSS had less effect with a $p = 0.0228$ [5].

A high prior surgical score has not been shown to affect prognosis with colon cancer. However, extensive prior dissection with rectal cancer in the pelvis has a profound effect on prognosis in treating peritoneal metastases. Sugarbaker reported a median survival of 35 months and a five-year survival of 40 % for colon cancer patients having a complete CRS. In contrast, rectal cancer patients having the same treatments had a median survival of 17 months and there were no long-term survivors [10]. Verwaal showed that the prognosis of

rectal cancer patients treated for peritoneal metastases was markedly reduced ($p = 0.069$) [7]. A similar phenomenon was reported by Yang et al. in the prospective randomized trial of gastric cancer patients treated with CRS and HIPEC for peritoneal metastases. Patients treated for primary gastric cancer with peritoneal metastases had twice the survival when CRS and HIPEC were used as compared to CRS alone. However, those patients who had CRS and HIPEC for recurrent gastric cancer with peritoneal metastases failed to show benefit [13]. If neoadjuvant intraperitoneal and systemic chemotherapy was used, the differences in synchronous versus metachronous patients with peritoneal metastases was absent [14]. Cancer cells entrapped in the pelvis as a result of rectal cancer surgery or within the left upper quadrant of the abdomen with gastric cancer cannot have a complete CRS because of tumor cell entrapment at anatomic sites impossible to dissect free of peritoneal metastases.

An extreme example of prognosis determined by PSS was reported by Look and Sugarbaker for ovarian cancer [14]. They studied the clinical features of 28 ovarian cancer patients who had CRS and HIPEC for recurrent ovarian cancer. As would be expected, complete versus incomplete cytoreduction was a significant feature ($p = 0.037$). However, PSS was an equally robust clinical feature determining prognosis ($p < 0.001$) (Fig. 5).

Fig. 5 Survival rates according to prior surgical score ($p < 0.001$) in patients with recurrent ovarian cancer. (From reference 14 with permission)

Preoperative CT

All patients being evaluated for CRS and HIPEC have a preoperative CT or MRI. In patients with non-mucinous cancer PET-CT is frequently obtained. The first priority in evaluating this study is the assessment of metastatic disease at systemic sites and in the liver. A second goal of preoperative CT is an assessment of the anatomic sites and lesion size of peritoneal metastases. Also, an estimate of visceral involvement is desired. This second assessment is referred to as the CT-PCI.

Jacquet and colleagues evaluated the abdominal and pelvic CT performed with both systemic and maximal oral contrast. The CT findings were recorded for all nine abdominopelvic regions. The size and number of each cancer nodule or mass was recorded. These observations were prospectively recorded for the CT and were compared to those observed at the time of abdominal exploration and during the cytoreductive surgical procedure. Figure 6 shows the results of this study [15].

Fig. 6 Influence of tumor volume on sensitivity of CT scan. Constructed from 783 observations in 45 patients. (From reference 15 with permission)

Small peritoneal nodules or masses less than 0.5 cm were detected at only 28 %. Moderate size nodules 0.5 to 5.0 cm were detected at 72 % and gross nodules greater than 5 cm at 90 %. These authors concluded that the accuracy of CT in peritoneal metastases was greatly dependent on lesion size. When the nine abdominopelvic regions were compared, the pelvic region was the least accurate.

Koh and colleagues performed a similar lesion by lesion analysis comparing preoperative CT with interpretative findings [16]. For lesion size less than 0.5 cm the sensitivity was only 11 %. For nodules 0.5 to 5.0 cm the sensitivity was 37 % and for nodules greater than 5 cm the sensitivity was 94 %. Koh et al. concluded that the sensitivity of CT was influenced by lesion size and that CT-PCI significantly underestimated the clinical PCI.

Yun and coworker published important observations concerning the CT-PCI in 76 patients [17]. The detection rate was highest for appendix peritoneal metastases (84 %) and lowest for gastric (47 %). The sensitivity of preoperative CT was influenced by histologic type (mucinous versus non-mucinous) tumor size and tumor location.

An example of the inaccuracy of the preoperative CT was demonstrated in a 60 year old woman had gastric cancer with signet ring morphology and a complete radiologic response to neoadjuvant chemotherapy. She developed gastric outlet obstruction approximately two months after completion of chemotherapy and was evaluated for palliative surgery. Laparoscopy showed a few minute peritoneal metastases. CT-PCI was zero. At surgery the clinical PCI was 18 and the cytoreductive surgery with total gastrectomy resulted in a postoperative PCI of 7 (Fig. 7). Figure 8 shows the peritoneal metastases diffusely penetrating into the subperitoneal lymphatic system of the small bowel mesentery.

The concept of concerning radiologic features identified on preoperative CT has been used to help select patients for complete cytoreduction. The list of 13 concerning radiologic features is shown in Table 1. Rivard and colleagues in their study of radiologic features reported that no single adverse image was associated with unresectability. However, it did have an impact on the outcome [18]. Statistically significantly patients with two or more concerning features were more likely to have a suboptimal cytoreduction (87.5 % for 2 features and 36.4 % for a single feature, $p = 0.035$).

The importance of concerning radiologic features was explored by Jacquet and colleagues for patients with mucinous peritoneal metastases being considered for cytoreductive surgery. Twenty-five patients with complete CRS were compared to 20 with incomplete CRS. The groups were assessed by presence versus absence of 16 CT radiologic features [19]. If a patient by preoperative CT had bowel segments obstructed by tumor, the complete CRS occurred in 12 %. If in addition tumor volume was equal to or greater than 0.5 cm on jejunum or upper ileum, no patients had complete CRS. Again in this

Regions	CT-PCI	Regions	PCI at Exploration	Regions	PCI Post Resection
0. Central	0	0. Central	2	0. Central	0
1. Right Upper	0	1. Right Upper	1	1. Right Upper	1
2. Epigastrium	0	2. Epigastrium	2	2. Epigastrium	0
3. Left Upper	0	3. Left Upper	1	3. Left Upper	1
4. Left Flank	0	4. Left Flank	1	4. Left Flank	0
5. Left Lower	0	5. Left Lower	2	5. Left Lower	0
6. Pelvis	0	6. Pelvis	2	6. Pelvis	1
7. Right Lower	0	7. Right Lower	1	7. Right Lower	0
8. Right Flank	0	8. Right Flank	1	8. Right Flank	0
9. Upper Jejunum	0	9. Upper Jejunum	1	9. Upper Jejunum	1
10. Lower Jejunum	0	10. Lower Jejunum	2	10. Lower Jejunum	1
11. Upper ileum	0	11. Upper ileum	1	11. Upper ileum	1
12. Lower Ileum	0	12. Lower Ileum	1	12. Lower Ileum	1
Preoperative PCI	0	Intraoperative PCI	18	Postoperative PCI	7

Fig. 7 60 year old woman with signet ring gastric adenocarcinoma of the stomach and increasing gastric outlet obstruction despite after complete clinical response to neoadjuvant chemotherapy

study two concerning radiologic features were associated with incomplete cytoreduction.

Yan and colleagues retrospectively studied 30 patients with peritoneal mesothelioma who had an adequate versus suboptimal CRS [20]. Thirty-nine CT parameters were scored in the two groups of patients. A decision tree analysis was performed. If the CT showed a tumor mass greater than 5 cm in the epigastric region a suboptimal cytoreduction occurred in 78 % of patients. In an absence of a tumor mass greater than 5 cm only 19 % had a suboptimal CRS. If patients had class III involvement of small bowel regions in addition to tumor size greater than 5 cm in small bowel regions the suboptimal CRS occurred in 100 % of patients. If both of these radiologic parameters were absent, the suboptimal CRS was only 6 %.

In summary, in these three radiologic studies of the impact of concerning radiologic features on complete versus incomplete cytoreduction, a single concerning radiologic feature indicated a reduced but not absent complete CRS. However, the identification of two concerning radiologic features indicated that an adequate CRS was very unlikely.

Response to Neoadjuvant Chemotherapy

In many clinical situations in the management of peritoneal metastases, neoadjuvant chemotherapy (NAC) is indicated prior to a final decision to perform CRS and HIPEC. The evidence that response to NAC predicts a favorable prognosis with CRS and HIPEC is well established. Bijelic identified 10 of 34 patients with appendiceal mucinous carcinoma with peritoneal metastases treated with NAC using FOLFOX who had a complete or near-complete response by a study of the tissue specimens resected [21]. Figure 9 shows the remarkable prolonged survival of patients who had a marked NAC response as compared to those with a partial or absent response.

Passot performed a similar study in colon or rectal cancer patients with peritoneal metastases who had a NAC prior to CRS and HIPEC. Twelve patients had a complete response, 23 had a major response and 80 had a minor or no response [22]. The three groups of patients had a marked difference in survival ($p = 0.0019$). These survival

Fig. 8 60 year old woman with signet ring adenocarcinoma of the stomach. At surgery peritoneal metastases were in subperitoneal lymphatics

Table 1 Concerning radiologic features observed on preoperative CT as a prognostic assessment for patients with peritoneal metastases

- Bowel obstruction or partial obstruction at more than one site
- Non-mucinous ascites
- Mesentery drawn together by tumor (clumped)
- Tumor infiltrating leaves of small bowel mesentery
- Mesenteric or para-aortic lymphadenopathy
- Porta hepatis involvement
- Hydroureter
- Psoas muscle invasion
- Gastric outlet obstruction
- Pelvic sidewall invasion
- Tumor ≥ 5 cm in lesser omentum or subpyloric space
- Tumor ≥ 5 cm in jejunal regions
- CT-PCI > 20 (excluding pseudomyxoma peritonei)
- Retroperitoneal lymphadenopathy
- Pleural effusion in the absence of extensive ascites

differences were determined by an assessment of histopathologic specimens removed at the time of CRS and HIPEC. They concluded that histopathologic response to NAC was a new prognostic tool for the management of peritoneal metastases from colorectal cancer.

In a study of gastric cancer with peritoneal metastases, Fujiwara performed serial laparoscopy to assess the effects of neoadjuvant intraperitoneal and systemic chemotherapy [23]. These patients in whom peritoneal metastases disappeared and

Table 2 Impact of response to neoadjuvant chemotherapy on outcome with CRS plus HIPEC in patients with peritoneal metastases from colorectal cancer. Borderline resectable patients given chemotherapy are separated into 3 groups

Complete Response (10 %)	No Response (70 %)	Partial Response (20 %)
CRS of value for staging, benefit from HIPEC questionable	Palliative benefit from resection, HIPEC may be of benefit if drugs used are changed from those used for NAC	Expect benefit from CRS and HIPEC

peritoneal nodules were no longer visible went on to have gastrectomy with CRS and HIPEC. This group of patients had a statistically significant improved outcome ($p = 0.0173$). A reliable evaluation of response to neoadjuvant chemotherapy in the absence of serial laparoscopy has not been published.

Changes in the level of tumor markers before and after NAC may be of help in the evaluation of response. This has been used as a reliable assessment of the extent of ovarian cancer using CA125 tumor marker. Carcinoembryonic antigen (CEA) and CA19–9 may change suggesting a response but the reliability of this decrease has not been determined. Also, there may be changes in radiologic imaging before and after NAC. However, in the absence of laparoscopy, a reliable indicator of response to NAC with published data regarding major response (true positive ratio) or lack of response (true negative ratio) have not been published.

Accurate data regarding the response to NAC would help in the preoperative assessment of patients who are considered for CRS and HIPEC. In Table 2, the benefits of CRS and HIPEC after NAC are summarized for patients with colorectal cancer. In those 10 % of patients who have a complete response, CRS and HIPEC are of questionable benefit for prolonging survival. Generous use of biopsies is helpful in staging but extensive peritonectomy or visceral resections are not indicated; HIPEC is not likely to be of value either. If complete response could be established by an accurate preoperative assessment, the exploratory laparotomy could be avoided.

In those 70 % of patients who have a minor response or no response, CRS and HIPEC may be of benefit but perhaps of reduced benefit. These patients should not be denied the possible benefits of CRS and HIPEC [16]. However, if multiple cycles of systemic FOLFOX chemotherapy have not caused a response, HIPEC with intraperitoneal oxaliplatin and systemic 5-fluorouracil is not indicated. A HIPEC regimen of mitomycin C or mitomycin C plus doxorubicin is a better plan. Again, an assessment of NAC response preoperatively would be of benefit.

Fig. 9 Kaplan-Meier survival analysis of 10 patients with PMCA from appendix cancer treated with neoadjuvant systemic chemotherapy prior to cytoreductive surgery and HIPEC who had a complete or near-complete histological response (median survival not reached) compared to 24 patients who had no significant histological response (median survival 29.5 months). The difference is statistically significant ($p = 0.032$). (From reference 21 with permission)

Table 3 Normograms to assess prognosis – Peritoneal Surface Disease Severity Score (PSDSS) (Pelz J, Surg Oncol, 2009)

Clinical symptom ^a	Extent of carcinomatosis	Primary hispathology
No symptoms (0 points)	PCI < 10 (1 point)	Well or moderately differentiated and N0 (1 point)
Mild symptoms (1 point)	PCI 10–20 (3 points)	Moderately differentiated and N1 or N2 (3 points)
Severe symptoms (6 points)	PCI >20 (7 points)	Poorly differentiated or signet cell (9 points)

PCI peritoneal cancer index

^a Symptoms: mild (weight loss <10 % of body weight, mild abdominal pain, asymptomatic ascites) or severe (weight loss ≥10 % of body weight, unremitting pain, bowel obstruction, asymptomatic ascites)

In those 20 % of patients with a major response that falls short of complete response, a reduced number of cancer cells will remain behind in scar tissue that was once cancer tissue. This may be a challenging CRS. The HIPEC should probably be the same as was used for NAC for a continued chemotherapy effect. Accurate information regarding a major response prior to CRS and HIPEC would be of benefit in planning the intervention.

Normograms

Three attempts to establish normograms to assess prognosis have been published to date. None has gained wide acceptance. However, the concept of a simple assessment that could preoperatively estimate the outcome after CRS and HIPEC would be of great utility. Verwaal et al. published the prognostic score (PS); this assessment used five prognostic features that were each assigned a constant number. The lower the score, the better the response [24].

Cashin and coworkers constructed their normogram from 9 different clinical variables. This COREP score varied from 0 to 18 with a low score indicating a poor prognosis [25]. Pelz and colleagues published data on the Peritoneal Surface Disease Severity Score or PSDSS [26]. The numerically weighted clinical symptoms, CT-PCI and primary cancer histology to calculate a score from 2 to 22 that would estimate the outcome expected from a CRS and HIPEC procedure (Table 3). The PSDSS has been used to estimate outcome for ovarian cancer as well as colon cancer.

Summary

A preoperative assessment of prognosis is required for improved management of patients with peritoneal metastases. The histopathology of the primary cancer and its peritoneal metastases is a requirement of the patient selection process. The PSS will give an estimate of the extent of tumor cell entrapment. Although the clinical PCI determined at the time of abdominal exploration is of great value in predicting the outcome of CRS and HIPEC, unfortunately an assessment of

the extent of disease by CT-PCI is not of sufficient accuracy to be useful.

The CT is of more use to identify the concerning radiologic features. One concerning radiologic feature indicates a reduced prognosis while two concerning radiologic features suggests that CRS and HIPEC will not achieve a complete CRS. Although difficult to assess preoperatively, response to NAC has a profound impact on prognosis and the way in which CRS and HIPEC should be administered. Normograms to estimate the success of CRS and HIPEC have been published; the normogram PSDSS is sufficiently simple and applicable in different diseases to merit further application.

References

1. Sugarbaker PH (1995) Peritonectomy procedures. *Ann Surg* 221: 29–42
2. Sugarbaker PH, van der Speeten K, Stuart OA, Chang D, Mahteme H (2012) Patient- and treatment-related variables, adverse events and their statistical relationship for treatment of peritoneal metastases. In: Sugarbaker PH (ed) *Cytoreductive surgery & perioperative chemotherapy for peritoneal surface malignancy. textbook and video atlas*. Cine-Med Publishing, Woodbury, pp. 183–206
3. Van der Speeten K, Stuart OA, Sugarbaker PH (2012) Pharmacology of perioperative cancer chemotherapy. In: Sugarbaker PH (ed) *Cytoreductive surgery & perioperative chemotherapy for peritoneal surface malignancy. textbook and video atlas*. Cine-Med Publishing, Woodbury, pp. 159–182
4. Harmon RL, Sugarbaker PH (2005) Prognostic indicators in peritoneal carcinomatosis from gastrointestinal cancer. *Int Semin Surg Oncol* 2(1):3
5. Sugarbaker PH (2012) Pseudomyxoma peritonei and peritoneal metastases from appendiceal malignancy. In: Sugarbaker PH (ed) *Cytoreductive surgery & perioperative chemotherapy for peritoneal surface malignancy. textbook and video atlas*. Cine-Med Publishing, Woodbury, pp. 57–78
6. Ihemelandu C, Sugarbaker PH (submitted for publication) Clinicopathologic characteristics and prognostic predictors of survival in patients with signet ring or adenocarcinoid adenocarcinoma of the appendix treated with cytoreductive surgery (CRS) and perioperative intraperitoneal chemotherapy: A single institution's experience
7. Verwaal VJ, van Tinteren H, van Ruth S, Zoetmulder FAN (2004) Predicting the survival of patients with peritoneal carcinomatosis of

- colorectal origin treated by aggressive cytoreduction and hyperthermic intraperitoneal chemotherapy. *Br J Surg* 91:739–746
8. Magge D, Zenati M, Mavanur A, Winer J, Ramalingam L, Jones H, Zureikat A, Holtzman M, Lee K, Ahrendt S, Pingpank J, Zeh HJ, Bartlett DL, Choudry HA (2014) Aggressive locoregional surgical therapy for gastric peritoneal carcinomatosis. *Ann Surg Oncol* 21(5):1448–1455
 9. Elias D, Gilly F, Boutitie F, Quenet F, Bereder JM, Mansvelt B, Lorimier G, Dube P, Glehen O (2010) Peritoneal colorectal carcinomatosis treated with surgery and perioperative intraperitoneal chemotherapy: retrospective analysis of 523 patients from a multicentric French study. *J Clin Oncol* 28:63–68
 10. Sugarbaker PH, Bijelic L (2016) Surgical procedures for peritoneal surface malignancy. In Khatri, VP (ed). *Atlas of Advanced Operative Surgery*. 2nd Edition. Elsevier
 11. Jacquet P, Sugarbaker PH (1996) Current methodologies for clinical assessment of patients with peritoneal carcinomatosis. *J Exp Clin Cancer Res* 15(1):49–58
 12. da Silva RG, Sugarbaker PH (2006) Analysis of prognostic factors in seventy patients having a complete cytoreduction plus perioperative intraperitoneal chemotherapy for carcinomatosis from colorectal cancer. *J Am Coll Surg* 203(6):878–886
 13. Yang XJ, Huang CQ, Suo T, Mei LJ, Yang GL, Cheng FL, Zhou YF, Xiong B, Yonemura Y, Li Y (2011) Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy improves survival of patients with peritoneal carcinomatosis from gastric cancer: final results of a phase III randomized clinical trial. *Ann Surg Oncol* 18:1575–1581
 14. Look M, Chang D, Sugarbaker PH (2004) Long-term results of cytoreductive surgery for advanced and recurrent epithelial ovarian cancers and papillary serous carcinoma of the peritoneum. *Int J Gynecol Cancer* 14(1):35–41
 15. Jacquet P, Jelinek JS, Steves MA, Sugarbaker PH (1993) Evaluation of computer tomography in patients with peritoneal carcinomatosis. *Cancer* 72(5):1631–1636
 16. Koh JL, Yan TD, Glenn D, Morris DL (2009) Evaluation of preoperative computed tomography in estimating peritoneal cancer index in colorectal peritoneal carcinomatosis. *Ann Surg Oncol* 16:327–333
 17. Yun LC, Yonemura Y, Ishibashi H, Sako S, Tsukiyama G, Kitai T, Matsuki N (2011) Evaluation of preoperative computed tomography in estimating peritoneal cancer index in peritoneal carcinomatosis. *Jpn J Cancer Chemother* 38:2060–2064
 18. Rivard JD, Temple WJ, McConnell YJ, Sultan H, Mack LA (2014) Preoperative computed tomography does not predict resectability in peritoneal carcinomatosis. *Am J Surg* 207:760–765
 19. Jacquet P, Jelinek JS, Chang D, Koslowe P, Sugarbaker PH (1995) Abdominal computed tomographic scan in the selection of patients with mucinous peritoneal carcinomatosis for cytoreductive surgery. *J Am Coll Surg* 181:530–538
 20. Yan TD, Haveric N, Carmignani P, Chang D, Sugarbaker PH (2005) Abdominal computed tomography scans in the selection of patients with malignant peritoneal mesothelioma for comprehensive treatment with cytoreductive surgery and perioperative intraperitoneal chemotherapy. *Cancer* 15:839–849
 21. Bijelic L, Kumar AS, Stuart OA, Sugarbaker PH (2012) Systemic chemotherapy prior to cytoreductive surgery and HIPEC for carcinomatosis from appendix cancer: Impact on perioperative outcomes and short-term survival. *Gastroenterol Res Pract* 2012 Article ID 163284:6
 22. Passot G, You B, Boschetti G, Fontaine J, Isaac S, Decullier E, Maurice C, Vaudoyer D, Gilly FN, Cotte E, Glehen O (2014) Pathological response to neoadjuvant chemotherapy: A new prognosis tool for the curative management of peritoneal colorectal carcinomatosis. *Ann Surg Oncol* 21:2608–2614
 23. Fujiwara Y, Takiguchi S, Nakajima K, Miyata H, Yamasaki M, Kurokawa Y, Okada K, Mori M, Doki Y (2011) Neoadjuvant intraperitoneal and systemic chemotherapy for gastric cancer patients with peritoneal dissemination. *Ann Surg Oncol* 18:3726–3731
 24. Canbay E, Mizumoto A, Ichinose M, Ishibashi H, Sako S, Hirano M, Takao N, Yonemura Y (2014) Outcome data of patients with peritoneal carcinomatosis from gastric origin treated by a strategy of bidirectional chemotherapy prior to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in a single specialized center in Japan. *Ann Surg Oncol* 21(4):1147–1152
 25. Cashin P, Graf W, Nygren P, Mahteme H (2013) Comparison of prognostic scores for patients with colorectal cancer peritoneal metastases treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *Ann Surg Oncol* 20:4183–4189
 26. Pelz JOW, Stojadinovic A, Nissan A, Hohenberger W, Esquivel J (2009) Evaluation of a peritoneal surface disease severity score in patients with colon cancer with peritoneal carcinomatosis. *J Surg Oncol* 99:9–15