

# Peritoneal carcinomatosis of colorectal cancer

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## ABSTRACT:

The incidence of peritoneal carcinomatosis of colorectal cancer amounts to 5%-15% for synchronous metastases and as much as 40% in cases of local recurrence. Despite significant advances in pharmacological treatment consisting in introduction of targeted medications, prognoses for patients with peritoneal metastases are still unfavorable. Mean survival of these patients undergoing palliative treatment is in the range of 6-9 months; overall survival rarely exceeds 2 years upon extensive chemotherapy. Markedly better results are obtained for cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (HIPEC). This treatment offers much better outcomes, leading to 5-year survival rates of as much as 30%-50%. The possibility to achieve such outcomes depends on the staging of peritoneal metastases as well as the completeness of macroscopic cytoreduction. The procedures require significant experience in abdominal surgery, are time-consuming (mean duration of the procedure ranging from 6 to 8 hours) and are burdened by complications that are due not only to the procedure itself but also to the intraperitoneal administration of the cytostatic drug at elevated temperature (41.5 °C). However, in patients with metastases limited to the peritoneum the procedure is justified by its outcomes. At the same time, combination of surgical cytoreduction with HIPEC followed by systemic chemotherapy offers a radical change in prognosis for patients hitherto qualified for palliative treatment only.

## KEYWORDS:

colorectal Cancer, peritoneal metastases, HIPEC, financial aspect

Peritoneal carcinomatosis of colorectal cancer occurs synchronously with the primary tumor in approximately 5 to 15 percent of patients [1-4] and in 60 % of them peritoneum is the sole site of metastatic disease [3]. Metachronous peritoneal carcinomatosis in this cancer type constitutes 20% to 25% of all metachronous metastases and occurs in 40% of patients with local recurrence of CRC [1,5,6].

In the past several years, the results of treatment of advanced CRC have improved due to introduction of novel cytotoxic drugs and targeted therapy. However, the results of treating PC of colorectal cancer were still not satisfactory and mean survival time rarely exceeded 6-9 months. Poor results of treating PC with systemic chemotherapy are also connected with limited availability of anti-cancer drugs delivered intravenously due to blood-peritoneum barrier. Studies conducted by Elias [7], Franko [8], Verwaal [9] and Mahteme [10] indicated improved survival of patients with colorectal cancer after cytoreductive surgery with HIPEC compared to surgery with systemic chemotherapy (Table I).

PC is the most common cause of treatment failure in CRC, resulting in ascites and/or ileus. This is further aggravated due to problems with early detection of metastases in peritoneum as they are significantly more difficult to diagnose than liver or lung metastases as medical images (CT, ultrasound, MRI) are often problematic to evaluate in the context of detecting small metastases. Detection of them in the stage where the patient reports clinical symptoms (increased abdominal girth, subileus) rarely allows for effective treatment – often, only symptomatic treatment is possible.

Colorectal cancer with peritoneal carcinomatosis is considered a systemic disease. This is reflected in TNM classification according to UICC (*Union Internationale Contre le Cancer*), where this stage is described as M1b (metastases in more than one organ or metastases to peritoneum). Although this is a negative predictive factor, among selected group of patients effective treatment may be used with results comparable to treating single liver metastases of CRC [18]. On the other hand, exclusively palliative treat-

ment in this group of patients only results in mean survival of 6-9 months [19]. Meta-analysis conducted by Cao *et al.* confirmed survival difference in favour of radical treatment (CRS+HIPEC) compared to palliative treatment ( $p<0.0001$ ) [20]. In 2003, Verwaal *et al.* published results of randomized trial where they compared results of treating patients with peritoneal carcinomatosis of colorectal cancer using standard protocol (palliative surgery + systemic chemotherapy) vs. those treated using cytoreductive surgery and HIPEC procedure [21]. The study has shown not only better results in patients who underwent radical treatment with hyperthermic perfusion intraperitoneal chemotherapy, but also better survival in patients with limited peritoneal carcinomatosis and in cases where full macroscopic cytoreduction of neoplasm was possible. Reevaluation of treatment results in 2008 has shown 45% of 5-year survival in patients who had undergone HIPEC and complete cytoreduction (CC-0), with mean observation period of 8 years [9].

A French study has evaluated the results of treatment in a selected group of 48 patients with CRC after cytoreductive surgery and HIPEC [7]. To create a group uniform with respect to assumed parameters, the group was selected from among 75 patients treated at five different centers. Patients qualified for this mode of treatment were in good condition, without severe clinical symptoms and aged under 66. Staging of PC was conducted by evaluating 4 quadrants of peritoneal cavity and additionally pelvis. During the surgery, before HIPEC, 5-FU and leucovorin were administered intravenously. Results were compared with those for patients with PC treated with palliative chemotherapy (standard) in the same time period. Five-year survival was observed in 51% of patients, while in the 'standard' group, treated with modern anti-cancer drugs, median survival was 24 months.

The results of this study are interesting when compared to those obtained in a multi-center study, where the treatment results of 523 cases with CRC and peritoneal carcinomatosis who underwent CRS and HIPEC were evaluated [24]. Those patients were treated at 23 centers. Complete cytoreductive surgery (CC-0) was

performed in 84% of patients, which – as shown through multivariate analysis – was major contributing factor to obtain good treatment results. The 3- and 5-year survival was, respectively, 41% and 27% and was visibly lower than in a selected group treated at a single, but specialized center [7]. Due to significant differences in the technical elements of HIPEC between centers, authors indicate the necessity of creating a common treatment standard.

In a study coming from another French center, results of treatment of PC in different disorders were examined. Among them, 80 cases with CRC who had CRS+HIPEC were analyzed [25]. The 3-year survival was achieved in 60.3% of patients, while the 5-year survival – in 37%. Statistical analysis has shown a strong correlation between survival time and extent of metastases evaluated with PCI scale, and completeness of cytoreduction (CC). An important result was the correlation between treatment results and technical aspects of cytoreductive surgery such as e.g. duration of surgery, number of units of blood administered, and number of Panastomoses performed. Interestingly, the number of organs removed from abdominal cavity had no influence on survival. The authors emphasize a high correlation between treatment results and experience of the team increasing with the number of surgeries performed (the learning curve of the team).

A study evaluating the experiences of a Danish center in Aarhus presents a group of 80 patients with PC, who had CRS+HIPEC procedure with the intention of inducing full remission, among whom the primary disease was CRC in 34 patients [9]. Authors emphasize worse treatment results than those presented in Dutch and French studies. However, they are significantly better than the alternative – palliative treatment. In the context of this work, we would like to underscore Polish results of treating PC in CRC in a group similar in size to the Danish study [30]. A group of 36 patients constituted 32% of all patients with PC treated with CRS+HIPEC in Lublin and Gdańsk (52/111), which is comparable to the Danish study (43%). Better treatment results in the 3-year period are worth highlighting, which, we hope, will also be mirrored in the upcoming analysis of 5-year survival.

Published results of a Belgian study [27] present 48 cases, among which 36 (75%) had PC during qualification for surgery due to CRC. In 12 of them (25%) the neoplasm has originated from the appendix. It might have influenced high survival in the examined 3-year period, as appendiceal cancer has better prognosis than other bowel cancers and is usually described as a separate clinical entity, together with pseudomyxoma peritonei. The authors observed a statistically significant difference in survival of patients with PSI < 15 points and PSI > 15 points, both with respect to total survival and recurrence-free survival. Using statistical methods, other factors contributing to the risk of treatment failure were metastases to the small intestine mesentery requiring segmental resection, extra-abdominal post-operative complications and metastases greater than 5 cm.

Another study from a center in Pittsburgh, USA [8] retrospectively describes results of treating patients with PC of colorectal carcinoma divided into two groups: 67 cases after CRS+HIPEC+systemic chemotherapy (experimental group), while 38 with PC (no clinical signs, with primary tumor excised, without complete cytoreduction) were given aggressive systemic chemotherapy (control group). The results strongly indicate that if possible, cytoreduc-

**Tab. I.** Comparison of treatment results in patients with peritoneal carcinomatosis of colorectal cancer after CRS+HIPEC vs. systemic chemotherapy

AUTHOR, YEAR	CRS+HIPEC			SYSTEMICCHTH			BIBLIOGRAPHY
	2 YEARS %	5 YEARS %	MEDIAN (MONTHS)	2 YEARS %	5 YEARS %	MEDIAN (MONTHS)	
ELIAS 2009							
Franco 2010	81	51	62,7	65	13	23,9	7
Verwaal 2008	66	41	34,7	41	5	16,8	8
Mahteme 2004	40	19		22	10		9
Mahteme 2004	60	28		10	5		10

**Tab. II.** Results of treating patients with PC CRC

STUDY	YEAR	NO. OF PATIENTS	SURVIVAL	
			3-YEAR	5-YEAR
Verwaal [9]	2008	54	57%	45%
Elias [7]	2009	48	81%	51%
Elias [16]	2010	523	41%	27%
Desantis [17]	2015	80	60,3	37,0
Iversen [24]	2013	34	47%	38%
Hompes [20]	2012	48	85%	b.d.
Franco [10]	2010	67	45%	25%
Cavaliere [21]	2011	146	26%	18%
Polkowski, Jastrzębski [19]	2014	36	72%	

tive surgery with HIPEC should be primarily taken into account. Median survival for both groups was 34.7 months vs. 16.0 months, respectively. Authors underline that the control group was not fully comparable to the experimental group: patients were older, liver metastases and PC were more common among them at the time of qualification for treatment. Differences were also observed in the range of anti-cancer drugs used in systemic chemotherapy: while there were no differences between the use of 5-FU and irinotecan, drugs such as oxaliplatin, bevacizumab and cetuximab were used more often in the experimental group. Authors conclude that systemic chemotherapy cannot be regarded as an alternative to hyperthermic intraperitoneal chemotherapy and vice versa, or that both of those treatment methods complement each other and should be used together as elements of multidisciplinary treatment of PC in colorectal cancer

Conclusions of American authors are supported by the study coming from five Italian centers [29]. A total of 146 cases with PC CRC were analysed, with 3-year and 5-year survival of 26% and 18%, respectively. In 31%, synchronous peritoneal metastases were observed, whereas in 69% - metachromous metastases. As much as 68% have been earlier treated with systemic chemotherapy. In the majority of cases, PCI was determined to be lower than 20 points, but in 18% the treatment was conducted with PCI > 20 points. CC-0 was achieved in 85%. All patients qualified for treatment were in good condition (ECOG 1-2). Patients disqualified from treatment were >76 years, in poor condition, or there was no possibility of cytoreduction in the peritoneal cavity. Analysing clinical data together with the presented results we must conclude that non-uniform selection of patients in the study does

**Tab. III.** Recommendations for treatment of PC in CRC

GUIDELINES	USA [25]	POLAND [27]	CANADA [28]
HIPEC mode	closed	Open, closed	Open, closed
Cytostatic drug, dose and perfusion time	Mitomycin C – 40 mg, 90 min	Mitomycin – 10 mg/L of liquid, 60–90 min Oxaliplatin – 460 mg/m <sup>2</sup> , 30 min	Mitomycin C, 40 mg, 60–90 min Oxaliplatin – 460 mg/m <sup>2</sup> , 30 min
Perfusion liquid temperature	42°C	41°C–43°C	43°C
<b>Qualification for cytoreductive surgery and HIPEC</b>			
ECOG	N/S	0,1	0,1
BMI	N/S	< 40	< 40
Age	N/S	< 65 years (66–74 years – individual evaluation)	< 70 years
PCI	N/S	< 20 pts.	< 20 pts.
CC	N/S	0	0
PSDSS evaluation	N/S	N/S	recommended

not allow to arrive at a strong conclusion, however it does seem to confirm results from other studies.

Cytoreductive surgery may cause complications depending on its scope, duration of the procedure and HIPEC, as well as many other factors. Treatment results are strongly correlated with the experience level of centers conducting them. Therefore, it is recommended that CRS+HIPEC surgery is performed at centers having extensive experience and performing them daily, which reduces post-operative complications as much as possible and allows to achieve best treatment results [31,32].

### Recommendations for treatment of colorectal cancer metastases in national and ESMO guidelines

Numerous studies conducted in the last 20 years and concerning combination therapy of peritoneal carcinomatosis originating from different neoplasms, including colorectal cancer, have led to standardization of treatment methods. This applies both to qualification of patients, intra-operative evaluation, scope of surgery and combination therapy with hyperthermic intraperitoneal chemotherapy (HIPEC).

Analysis of treatment standards conducted by therapeutic teams associated in the American Society of Peritoneal Surface Malignancies (ASPSM) resulted in creation of common guidelines on HIPEC procedure in colorectal cancer patients [25]. Parameters of HIPEC method such as type (open, closed), temperature of administered liquid, volume of perfusion liquid, kind of antineoplastic drugs and their dosage and duration of perfusion were evaluated. The consensus recommendation is: using closed administration, 40 mg of mitomycin C given as antineoplastic drug, perfusion time of 60 min, volume of perfusion liquid: 3 L, temperature of administered liquid 42°C [Tab. III].

In Poland, recommendations for the HIPEC procedure are described in the guidelines of the National Consultant for Oncologic Surgery (*Krajowy Konsultant Chirurgii Onkologicznej*) [26] and detailed by a team of specialists [27]. Following treatment recommendations were made for PC in CRC: patients' qualification: stage of peritoneal carcinomatosis < 20 PCI, possibility of a complete cytoreduction (CC-0), general condition over 2 according to ECOG; HIPEC method: open or closed, drugs chosen depending on primary tumor; for CRC oxaliplatin or mitomycin C is advised,

temperature of administered liquid 41°C–43°C, perfusion time dependent on drug from 30 to 60 minutes.

Guidelines developed by the Canadian HIPEC Collaborative Group (CHICG) are generally similar to the established standards of treatment, including the above [28]. Canadian authors have extended their guidelines with detailed information on the qualification of patients to surgery, such as age, Body Mass Index, thereby strengthening the qualification criteria and including dependence on individual evaluation. They have indicated a need for carefulness in creating anastomoses in the left hemicolon region and anastomoses of the rectum. Such anastomoses are regarded as high-risk and authors recommend creating a protective stoma.

Recommendations concerning treatment of PC CRC were originally included in the ESMO (European Society of Medical Oncology) guidelines. Being very general, the guidelines underlined the importance of careful qualification of patients for this method of treatment, including good general condition, limited spread to the peritoneum (PCI < 20 pt) and possibility of complete cytoreduction. They also advised performing this procedure only at specialized centers with extensive experience, characterized by among others low percentage of post-operative complications and low mortality rate [29]. The most recent ESMO guidelines pointed to cytoreductive surgery with HIPEC as a method that should be used increasingly widely, and described its use as "being on the verge of becoming a standard" [30].

### Systemic chemotherapy as an adjunct to treatment with cytoreductive surgery and HIPEC

In the review by Waite *et al.* [31], 16 studies fulfilling the set criteria were evaluated, concerning both neoadjuvant and adjuvant chemotherapy. In 7 of them, regarding neoadjuvant therapy, no improvement was observed, with one study reporting worsening of prognosis. Fourteen studies investigated the use of adjuvant chemotherapy. No evident improvement of treatment outcome was observed following CRS and HIPEC. The authors conclude that using adjuvant chemotherapy might improve outcomes in patients with peritoneal carcinomatosis of colorectal cancer but evaluation of its efficiency requires further randomized studies.

A study by Devilee *et al.* [32] published in 2016 presents outcomes of 91 patients with synchronous peritoneal carcinomatosis, treat-

ed with cytoreductive surgery CC-0/1 with HIPEC. Among them, 25 (28%) have been treated with chemotherapy prior to surgery. In 96% of cases FOLFOX or CAPOX regimen was used. Seven patients additionally received bevacizumab. Reduction of spread of the disease evaluated using imaging techniques (CT, MRI or PET) was observed with PCI classification. The 3-year survival of patients who received systemic chemotherapy prior to surgery was 89%, compared to 50% among patients who received neoadjuvant chemotherapy ( $p < 0.01$ ). Authors conclude that patients who received systemic chemotherapy that lowered the stage of metastases to peritoneum show better results following CRS+HIPEC than patients who received systemic chemotherapy post-operatively.

Franco *et al.* [8] studied outcomes of patients with peritoneal carcinomatosis of colorectal cancer after cytoreductive surgery compared to those that were treated solely with systemic chemotherapy. Authors observed a statistically significant difference in the outcomes of patients treated with CRS+HIPEC+systemic chth (mean survival of 34.7 months vs. 16.8 months,  $p < 0.001$ ). Concluding, authors saw a benefit in using novel antineoplastic medications (irinotecan, oxaliplatin, bevacizumab) as opposed to 5-FU in systemic chemotherapy of patients with peritoneal carcinomatosis of CRC, especially when used with CRS+HIPEC. Evaluating their outcomes, the authors stated that systemic chemotherapy and HIPEC were not competing but complementary methods in the treatment of this stage of the disease.

### Qualification to cytoreductive surgery and HIPEC in peritoneal carcinomatosis of colorectal cancer

While peritoneal carcinomatosis of colorectal cancer is an indication for performing cytoreductive surgery and HIPEC, proper qualification of patients is a key to achieve expected treatment outcomes. In the aforementioned national and international guidelines, there are general recommendations on selection of patients, basing on the experience of teams using this treatment method and on literature analysis.

Most important elements in qualification of patients for CRS+HIPEC are, among others:

- no metastases except for peritoneum<sup>(a)</sup>
- good overall condition ( $> 70$  pts in Karnofsky scale)
- age  $< 70$  <sup>(b)</sup>
- peritoneum carcinomatosis spread according to PCI scale  $< 20$  pts<sup>(c)</sup>
- possibility of macroscopically complete cytoreduction (CC-0)

<sup>(a)</sup> – except for liver metastases (not more than 3)

<sup>(b)</sup> – individual selection, in some cases up to 75 years

<sup>(c)</sup> – according to some authors  $< 15$  pts.

Qualification of patients suffering from PC on the basis of the above allows for preliminary evaluation of possibility of surgery with the lowest risk of complications of the treatment process as compared to the expected benefits. In order to more precisely evaluate the expected outcome, PSDSS scale is used increasingly often [33,34,35]. This scale utilizes information available prior to decision on whether to treat a patient surgically. These are:

1. clinical evaluation for the presence of signs and symptoms indicating intraabdominal metastases
2. staging of peritoneal carcinomatosis according to PCI scale, using medical imaging techniques (Fig. 1)
3. histological evaluation of primary tumor

Staging using this scale involves the summation of points ascribed to each of the evaluated parameters. On that basis, we may differentiate 4 different stages, with each of them having been assigned particular prognosis values, based on clinical studies. An important point in the guidelines is that only PSDSS stages I – III should be operated with CRS + HIPEC. There is no clinical justification for performing this procedure in stage IV patients [34].

Next basic element of qualification of PC patients is staging with PCI (Peritoneal Cancer Index) scale (Fig. 1). All of current guidelines set the cut-off point for conducting cytoreduction and HIPEC at 20 pts. in this scale. Patients at a stage of over 20 pts. do not show a positive outcome of such treatment, but are exposed to a risk of complications from both surgical and HIPEC treatment. The relationship between both the outcome and survival duration is linearly dependent on the stage of PC in PCI scale [36]. Some authors stipulate to reduce the upper score limit during qualification to 15 pts. [20], however all current guidelines, including Polish, set the cut off at 20 pts.

### Cytoreductive surgery in the treatment of peritoneal carcinomatosis of colorectal cancer

A condition of obtaining a good outcome in cases of peritoneal carcinomatosis of colorectal cancer is not only a proper qualification of patients but, more importantly, possibility of performing macroscopically radical cytoreductive surgery [9, 37-39].

As soon as the surgery has commenced, after the abdominal cavity has been opened, staging of PC using PCI scale should be performed and possibility of successful surgery evaluated. Scope of cytoreductive surgery depends on the progression of metastases in parietal and visceral peritoneum. To achieve radical removal, it may be necessary to excise [40]:

parietal peritoneum (peritoneum covering diaphragm on the left and right side, parietal peritoneum, peritoneum covering the pelvic floor and right and left iliac fossa)

- greater and lesser omentum
- partial or complete colectomy
- upper rectum
- spleen
- part of urinary bladder wall
- gallbladder
- partial, segmental, small bowel resection
- excision of tissue located at the liver edge
- excision of liver capsule
- resection of uterus and ovaries in women
- marginal resection of stomach

During surgery, creation of colostomy or ileostomy is often necessary – the patient should be informed about such a possibility in advance. It is recommended to create no more than two bowel anastomoses due to the number of complications increasing together with the number of anastomoses. In case of anastomosis of the small or large intestine with the rectum, creating a protective ileostomy is recommended. Complications arising from the scope of surgery are possible, thus it is imperative to evaluate the possibility of performing the whole, radical procedure before its commencement. Cytoreductive surgery is technically hard and long in duration – average time of the procedure is 6-8 hours [].



**Tab. IV.** PSDSS (Peritoneal Surface Disease Severity Score) evaluation

CLINICAL EVALUATION	PCI EVALUATED USING IMAGING TECHNIQUES (OR DURING LAPAROTOMY)		TUMOR HISTOLOGY
NO SYMPTOMS 0 pts.	PCI < 10	1 pt.	G1-2, N (-), L (-), V (-) 1 pt.
MILD SYMPTOMS 1 pt.	PCI 10–20	3 pts.	G2 and at least one of N+, L+, V+ 3 pts.
SEVERE SYMPTOMS 6 pts.	PCI > 20	7 pts.	Every G3 Every signet ring 9 pts.

Explanations

MILD SYMPTOMS: moderate ascites, controlled abdominal pain, body mass loss < 10%

SEVERE SYMPTOMS: ileus, symptomatic ascites, poorly controlled abdominal pain, body mass loss > 10%

N – metastases to lymphatic nodes: (-) – absent, (+) – present

L – invasion of lymphatic vessels: (-) – absent, (+) – present

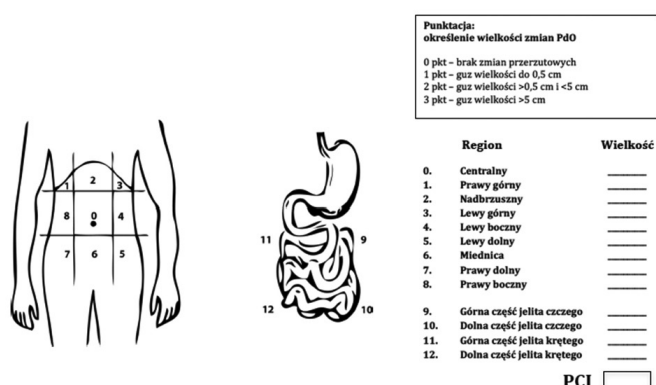
V – invasion of blood vessels: (-) – absent, (+) – present

Total number of pts.

Stage according to PSDSS

2–3	I
4–7	II
8–10	III
> 10	IV

Rycina 1. Ocena stopnia zaawansowania przerzutów do otrzewnej (PCI – Peritoneal Cancer Index)



**Fig. 1.** Klasyfikacja Sugerbakera przerzutów do otrzewnej (PCI – Peritoneal Cancer Index).

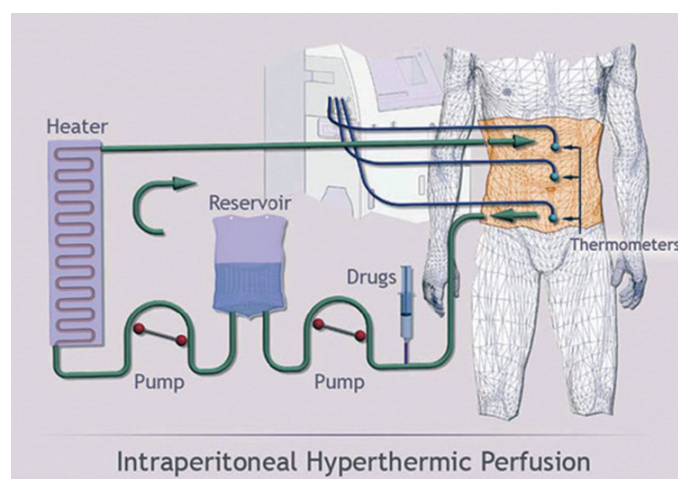
## Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

Following cytoreductive surgery, drains for delivery and removal of perfusion liquid are placed. The liquid is usually saline (when using mitomycin C) or 5% glucose solution (when delivering oxaliplatin). Dosage of relevant medicines is presented in Tab. V.

Additionally, thermometers are installed in the peritoneal cavity to measure the temperature inside the pelvis, in the subphrenic space and mid-bowel.

The procedure may be performed using one of two techniques: open (so called “Colosseum technique”) or closed, where the abdominal cavity is closed for the duration of perfusion or finally.

Approximately 3 L of perfusion liquid are delivered. After filling the peritoneal cavity and reaching target therapeutic temperature of 41–42 °C, (43 °C in delivery drain) [38], cytostatic drug is added to the circulating liquid. Perfusion time is 30 min (oxaliplatin) or 60–90 min (mitomycin C). Intraperitoneal administration of cy-



**Fig. 2.** Schemat wykonania dootrzewnowej chemioterapii perfuzyjnej w hipertermii. (Za pozwoleniem i dzięki uprzejmości firmy RanD, Modena, Włochy).

tostatic drugs at therapeutic doses allows to achieve significantly larger concentration of the drug in the peritoneal cavity than with intravenous delivery.

Next, cytostatic drug-containing liquid is removed through the efferent drain and clean saline is administered to clean the peritoneal cavity from remainder of cytostatic drugs. This liquid is also removed. After the perfusion, anastomoses of the gastrointestinal tract are created (anastomoses are done AFTER perfusion, not BEFORE). If an anastomosis with the rectum is required, a protective ileostomy is recommended. A schematic diagram of hyperthermic intraperitoneal chemotherapy is presented (Figure 2).

## Early postoperative intraperitoneal chemotherapy (EPIC) after CRS and HIPEC treatment

Some centers utilize postoperative chemotherapy through drains left in the peritoneal cavity (EPIC – Early Postoperative Intraperitoneal Chemotherapy) [39,41]. On 2<sup>nd</sup> – 6<sup>th</sup> day after surgery, cytostatic 5-fluorouracil at a dose of 500–650 mg/m<sup>2</sup> with 50

mEq of sodium bicarbonate is delivered intraperitoneally. Data regarding therapeutic outcomes of combining CRS+HIPEC+EP-IC are inconclusive and have both proponents and opponents [39, 41, 45]. It is however worth underlining the higher number of complications at stage III/IV, connected with EPIC use [45]. Nowadays, most centers do not perform EPIC following cytoreductive surgery and HIPEC.

## CONCLUSION

Numerous studies on the efficacy of treating patients with peritoneal carcinomatosis, including cases of colorectal cancer, indicate that these metastases should rather be treated as regional and not systemic.

Performing cytoreductive surgery with hyperthermic intraperitoneal chemotherapy leads to improvement of survival results in a selected group of patients compared to systemic chemotherapy alone [7,8,9]. On the other hand, peritoneal carcinomatosis when distant metastases are present is a negative prognostic factor, even in cases where systemic chemotherapy was administered [45, 46].

Systemic chemotherapy should not be regarded as alternative treatment method, but as an addition to surgical treatment and HIPEC as adjuvant therapy [8]. However, to confirm its efficacy in treatment of peritoneal carcinomatosis in conjunction with CRS+HIPEC further randomized studies are needed [31,32].

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**Tab. V.** Antineoplastic drugs used for HIPEC during treatment of peritoneal carcinomatosis of colorectal cancer

NAME OF THE DRUG	DOSE	PERFUSION TIME (MIN)	BIBLIOGRAPHY
Mitomycin C	10 mg/m <sup>2</sup>	60	[40, 43]
Mitomycin C	15 mg/m <sup>2</sup> (*)	60	[39]
Mitomycin C	40 mg	90	[25]
Mitomycin C	10 mg/L	60–90	[27, 28]
Oxaliplatin	460 mg/m <sup>2</sup> (*)	30	[27, 28, 41]
Cisplatin	25 mg/m <sup>2</sup> 3,3 mg/m <sup>2</sup> /l	60	[42]
Mitomycin C			

(\*) in conjunction with Early Postoperative Intraperitoneal Chemotherapy (EPIC)

A condition for achieving best treatment results of peritoneal carcinomatosis is proper qualification of patients and possibility of complete cytoreduction.

Most advanced stage allowing for both macroscopic completeness of removal and positive treatment outcome is 20 pts. in PCI scale (Peritoneal Cancer Index).

Hyperthermic Intraperitoneal Chemotherapy (HIPEC) may be performed both in an open and closed fashion.

Most commonly used antineoplastic drugs during HIPEC procedure are mitomycin C (at 40 mg/L or 35 mg/m<sup>2</sup>) and oxaliplatin (at 460 mg/m<sup>2</sup>) [38].

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