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Observations from the Working Group Peritoneal Carcinosis

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Abstract

The aim of this report was to describe the feasibility, overall survival and quality of life of combining multimodal therapy with a complementary therapy concept called LOTUS Care Cure program. The peritoneal carcinomatosis (PC) working group described their observations on the combination of multimodal therapy with a complementary therapy concept based on 132 patients with different cancer entities with suspected PC. PC was not confirmed by laparoscopy in 32.5% of the patients included in the working group of patients with suspected PC. Patient compliance and the feasibility were high. For Ki67, there is a cut-off at 45% with a slower progression at <45% and a faster progression of the disease at >45%. The higher the Karnofsky index, the more improved the therapy and tolerability, with a cut-off of 80%. Overall, 72.0% of patients died. The median survival time in the overall population was 3.74 years (95% CI, 2.57 to 4.91) with a sharp decline in the first 16 weeks. The quality of life of patients can be improved with the implementation of the complementary LOTUS Care Cure Project. Overall, the therapy of PC requires a multi-professional team of therapists and a multimodal therapy concept. The multimodal concept together with the Lotus Care Cure project shows very good feasibility with high compliance and ultimately leads to better and low-risk patient care.

Keywords

Multimodal and Complementary Therapy, Peritoneal Carcinosis, Quality of Life

1. Introduction

Peritoneal carcinosis working group observations Ayurveda is an ancient Indian system of medicine. The conception of the human body is based on five sheaths, one of which is assumed to be the peritoneum.

The anatomical knowledge about the peritoneum is available, but not about its functions or the mechanisms to maintain the functions or to cure it in case of diseases. Accordingly, in the case of advanced tumour disease with peritoneal carcinomatosis (PC), it is difficult to make statements about one or more possible therapeutic measures.

PC, which is a common manifestation of gynaecological and gastro-intestinal tract advanced cancers including ovarian cancer, colorectal and gastric cancer or appendicle tumour, has long been considered the final stage of a metastatic cancer. Prognosis is basically very poor with patients suffering from PC of gastric origin having a median survival estimate of 1 - 3 months [1] [2] while those having untreated colorectal peritoneal metastasis were reported to have a median overall survival of just 6 months [3]. For women with stage III invasive epithelial ovarian cancer, the average 5-year survival rate was reported to be 39% [4].

However, some therapeutic measures have developed in recent years, such as the Sugarbaker surgery [5] or pressurized intraperitoneal aerosolized chemotherapy (PIPAC) [6]. In 2010, the tricyclic antibody Removab became available as a method for intraperitoneal application using a catheter system. Unfortunately, the methods are not yet established.

There is increasing evidence that patients can benefit and even be treated from the so called multimodal therapy comprising of surgery to remove the peritoneum, systemic chemotherapy and hyperthermic intraperitoneal chemoperfusion (HIPEC) [7] [8]. Survival rate for selected patients with PC has been increased depending on the origin and histology of the tumour [9] [10] [11] [12] [13].

Next to the conventional treatment, there is increasing evidence regarding the beneficial effects of adjuvant complementary therapies comprising Ayurveda but also yoga, relaxation techniques, music therapy, nutritional counselling and supplementation on cancer and cancer treatment associated symptoms but also on physical and emotional well-being. Until now, clinical studies investigating complementary therapies have mainly focused on single treatment procedures, e.g. intake of dietary supplements [14] or herbal preparations [15] [16], gentle touch [17], acupuncture [18] or yoga [19]. However, there is conflicting evidence regarding the beneficial effects of certain procedures such as acupuncture [18] [20] [21] [22] or mistletoe extracts [15] [16] [23]. Furthermore, the effects of combining different procedures showed promising outcomes regarding fatigue, depression, and anxiety, appetite, sleep or overall well-being and quality of life [24] [25] [26] [27] [28]. One of these combination therapies is the complementary LOTUS Care Cure Project aiming to train outpatients already during the course of the disease and in parallel with the adjuvant or palliative therapies to develop

novel strategies to deal more successfully with their disease [28]. The program comprises of yoga, massage, physiotherapy, relaxation, art therapy, and psychological modalities as well as nutrition counselling and is being conducted by an interdisciplinary team of physicians, physiotherapist, nurses, health trainers, psychologists, nutritionists, and yoga teachers.

The present report aimed in describing the feasibility and overall survival rate and quality of life of the combination of a multimodal therapy with the LOTUS Care Program in patients suffering from PC from different primary tumours [28]. The working group for peritoneal carcinosis consisting of haemato-oncologist, internists, palliative physician, surgeon, pathologist, general practitioner, radiotherapist, naturopathic medicine, and pharmacist but also nutritionists, physiotherapists and others describe below their observations based on 132 cases.

2. Materials and Methods

2.1. Patient Group

132 patients of all sex, age and tumour entity with suspected peritoneal carcinosis were treated in the working group "Arbeitskreis Peritonealkarzinose" (PK) in the period from July 2014 to 2019.

Patients were included if they had Karnofsky performance status scale not <50, no need for nursing care, good compliance, understanding the German language/translator, and a suspected diagnosis of peritoneal carcinosis, which was based on a radiological report. The appearance of ascites was irrelevant. Patients who refused pain therapy were excluded from the therapeutic measures.

Anamneses included the recording of pre-existing conditions; laboratory chemical and electro-cartographic examination of the existing organ reserves with regard to the therapy measures planned later.

Patients were presented to a surgical team if Karnofsky-Index was at least 80% and if compliance was given. All patients provided written informed consent for involvement in the observation. The observations presented in the paper were collected in everyday clinical practice and therefore, no ethics vote was obtained.

2.2. Diagnostics and Treatment

Overview of the applied workflow of the diagnostic and treatment approach for PC is shown in **Figure 1** and **Figure 2**. The flowchart in **Figure 1** has been developed by the working group in 2014/2015 while the diagnostic workflow as shown in **Figure 2** was developed in 2018. Before evaluation of therapeutic measures, detailed histopathological confirmation of the diagnosis of peritoneal carcinomatosis was performed. Start of the observation was the laparoscopy where patients were also asked to fill in the German version of the EORTC QLQ-C30 questionnaire.

For the assessment of the peritoneal carcinomatosis regarding size and regional growth, laparoscopy was carried out. Under video documentation, tissue

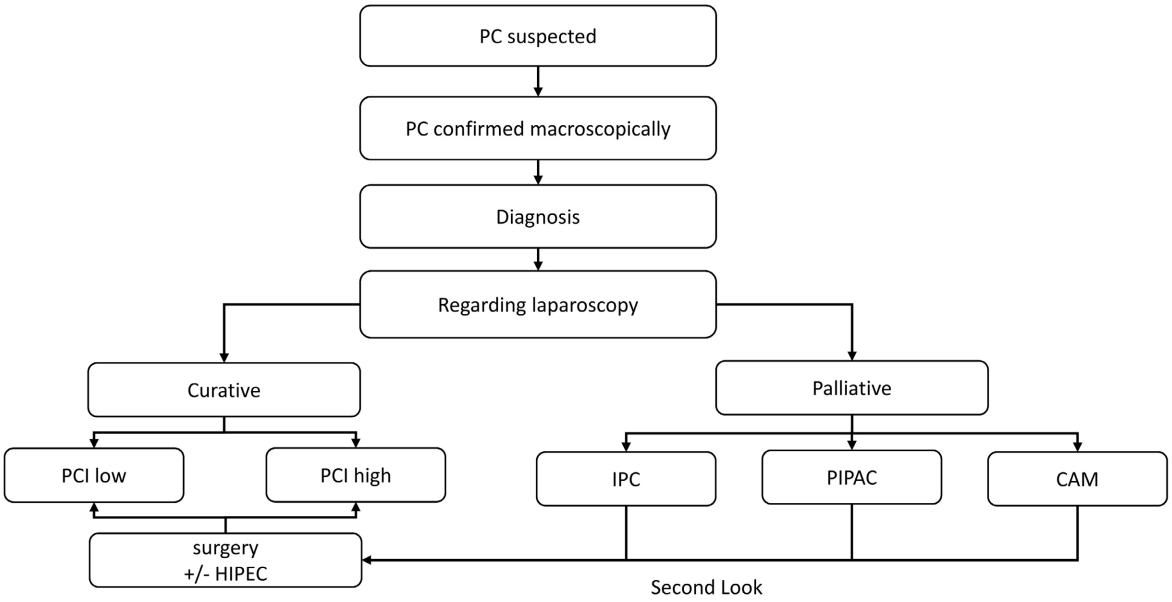

Figure 1. Flowchart: Working group peritoneal Carcinosis.

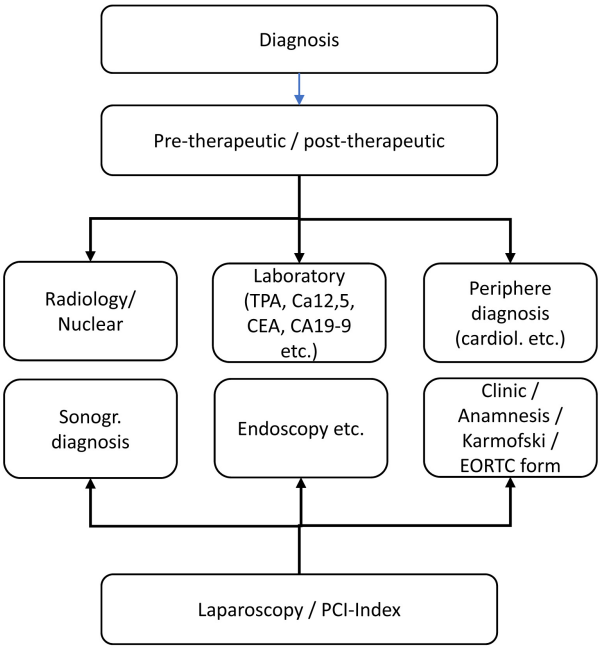

Figure 2. Flowchart: diagnosis.

samples were taken from all affected regions of the peritoneum in accordance with the Peritoneal Carcinoma Index (PCI).

Ascites that may be present are preserved, quantified and sent in total for histological examination. The catheter system is then carried out according to Tenckhoff. In case of unclear macroscopic findings, a short consultation with the treating oncologist was carried out.

Six months after the first systemic and intraperitoneal chemotherapy, the therapeutic response assessment took place using the second look laparoscopy.

2.3. Outcome Measures

The histological examination of the peritoneum includes the information according to the TNM staging system and the Ki67 labelling index to assess the proliferation activity. Further, immunohistochemical examinations up to of the PDL-1 expression were done.

The German version of the EORTC QLQ-C30 version 3 (German Cancer Society "Deutsche Krebsgesellschaft") was used [29]. The EORTC QLQ-C30 is a self-reported questionnaire that was developed to assess the quality of life of cancer patients and covers the most important dimensions of the health-associated quality of life and the most frequent symptoms as well as aspects of financial burden. The EORTC questionnaire was filled in before laparoscopy (0), before application of the first intraperitoneal chemotherapy (A), after 8 weeks (B), after 16 weeks (C).

2.4. Treatment

After laparoscopy, patients were referred to the oncologist to perform the systemic combined with the intra-peritoneal chemotherapy in case PC was diagnosed. The preparations for the administration of I.V. (also via port) + intraperitoneal (I.P., always via Tenckhoff catheter) therapy include vital measurements (RR, pulse, O2, blood sugar, height and weight), measurement of the abdominal circumference and three-day pain therapy over 3 - 4 hours consisting of: Dolantin, Tramal, Buscopan, Novalgin B12 and MCP. On the third day, the same cocktail without Dolantin was administered. Pain management is an essential and non-variable or negotiable component of systemic and local chemotherapy (CTh).

Basically, the multimodal therapy combines cytoreductive surgery (CRS) with hyperthermic intra-peritoneal chemotherapy (HIPEC) and systemic combination (SC) therapy.

The intra-peritoneal chemotherapy was administered as follows: infusion of 500 - 1000 ml NaCl solution, followed by liposomal doxorubicin (Caelyx)/dissolved in 500 ml. The weight-adapted amount escalates from 30 - 45 - 60 mg. After completing the local installation, the patient was asked to make a consistent change of position for 3 - 4 hours. It is then done after measuring the abdominal circumference again and draining the intra-abdominal therapy fluid. The systemic chemotherapy followed standard therapy regimes. The repetition of the intraperitoneal Caelyx application follows the repetition regime of the systemic therapy initially carried out once a week for six weeks.

The monitoring of the entire course of the local and systemic chemotherapy was carried out by laboratory chemistry (organ reserves, tumour markers) [30] and corresponding sonographic or radiological control examinations.

Further, oncological therapy depended then on the medical finding. In the event of complete regression of peritoneal carcinosis, the patient received only an abdominal irrigation with 1000 ml of table salt for system therapy and the cytological examination of the ascites then removed at regular intervals.

2.5. Complementary Therapy

In addition, and depending on the general condition of the patient as well as the Karnofsky index, all patients were offered further therapy methods such as the oncological complex treatment according to the Lotus Care Cure concept [28], local hyperthermia, possibly combined with complementary therapy or the administration of parenteral nutrition.

The Lotus Care Cure concept is a program comprising different conversation modules, foot reflexology, relaxation, nutrition counselling, art therapeutic painting, physiotherapy, yoga, psycho-oncologic sessions, and healing massage, and was conducted by an interdisciplinary team of physicians, physiotherapist, nurses, health trainers, psychologists, nutritionists, and yoga teachers. The main goal of this nonstationary outpatient program was to train patients already during the course of the disease and in parallel with the adjuvant or palliative therapies to develop novel strategies to deal more successfully with their disease. The program covered 3 weeks and was conducted mainly as a group therapy with a participant number of 6 - 8. A detailed description of the program is described in more detail elsewhere [28].

2.6. Statistics

Statistical analysis was performed using SPSS, version 27 (SPSS, Chicago, IL, USA). p-values < 0.05 were considered significant. The non-parametric Mann-Whitney U test for comparison of metric and ordinal variables between groups was used (pU), and for proportion values the exact Fisher test was calculated (pexF). Survival analysis was performed using the Kaplan–Meier method, and compared using the log-rank test.

3. Results

A total of 132 patients with different cancer entities including 65.3% women were treated. The characteristics of the included patients, treated by the working group, are summarized in **Table 1** and **Table 2**.

PC was only confirmed by laparoscopy in 67.5% of the patients included in the working group. Even though previously diagnosed with PC, PC finding was not confirmed in 32.5% of the cases. Patients without PC remained in the working group receiving all therapies apart from those related to the PC. 68.5% of patients with PC and 67.4% of those without PC had metastases. Overall, there was a high level of patient compliance and the feasibility was also given incl. patients with PCI > 20 (data not shown). The amount of ascites drainage decreased parallel to the tumour reduction in peritoneal carcinosis and the resumption of organ function.

For Ki67 there is a cut off at 45% with a slower course at <45% and a faster course of the disease at ≥45%. A change in Ki67 in response to therapy was examined during the second look-log laparoscopy, with all macroscopically abnormal regions being examined again histopathologically. The working group

Table 1. Characteristics of the study population at entry to the working group "Peritonealkarzinose".

Entity	All; n, %	With PC					Without PC			
		Entity with PC; n, %	Metastasis (%)	PCI value[a]; n	Ki67 category[a]; n	Karnofsky Index[a]; n	Metastasis (%)	PCI value[a]; n	Ki67 category[a]; n	Karnofsky Index[a]; n
All	132	89	68.5	11.0 (4.8, 19.0); 70*	35.0 (20.0, 60.0); 45	80.0 (70.0, 90.0); 82	67.4	0.0 (0.0, 8.5); 9	17.5 (14, 70); 4	80.0 (70.0, 90.0); 43
Colon	24, 12.2%	15, 62.5%	80.0	7.0 (3.0, 17.0); 11	60.0 (20.0, 70.0); 7	90.0 (80.0, 90.0); 13	55.6	4.0 (0, 28); 3	-; 0	80.0 (80.0, 90.0); 7
Gastric	13, 9.8%	10, 76.9%	50.0	6.0 (0.5, 16.0); 7	50.0 (26.0, 75.0); 5	80.0 (72.5, 87.5); 8	66.7	0.0; 1	-; 0	80.0 (70.0, 90.0); 3
GI[#]	12, 9.1%	10, 83.3%	70.0	10.5 (6.2, 18.0); 8	35.0 (20.0, 60.0); 7	75.0 (67.5, 90.0); 10	50.0	-; 0	19.0; 1	(80, 90); 2
Pancreas	23, 17.4%	12, 52.2%	75.0	15.5 (8.5, 20.5); 10	60.0 (25.0, 62.5); 6	80.0 (70.0, 88.8); 12	81.1	(2, 13); 2	-; 0	80.0 (77.5, 90.0); 10
Mamma	23, 17.4%	15, 65.2%	73.3	6.0 (0.5, 16.0); 13	20.0 (18.0, 40.0); 7	80.0 (70.0, 82.5); 14	75.0	-; 1	(14, 70); 2	75.0 (70.0, 87.5); 4
Ovarium	12, 9.2%	23, 92.0%	60.9	12.0 (5.0, 19.5); 17	25.0 (10.0, 70.0); 11	90.0 (80.0, 90.0); 21	50.0	-; 0	-; 0	(80.0, 90,0); 2
Others:	12, 9.2%	4, 66.7%	75.0	-; 1	-; 0	90.0; 1	62.5	-; 1	16.0; 1	80.0 (70.0, 90.0); 7
Lung cancer	4									
Base of the tongue	1	1								
Primary peritoneal	1	3								
Peritoneum	3									
Prostate	3									

[a]Data are given as median (1st, 3rd quartile); *pU < 0.05 between patients with and without PC; #GI incl. liver, gall bladder, neuroendocrine tumour.

Table 2. Age distribution of patients at first diagnosis, at PK diagnosis and at entry to the working group "Peritonealkarzinose" per cancer entity.

Entity	First diagnosis, yrs; (n = 132)	PC diagnosis, yrs; (n = 89)	Entry to PC working group, yrs		Time between first diagnosis and entry to PC working group, in months	
			With PC; n	Without PC; n	With PC; n	Without PC; n
All	62.2 (51.2, 69.7)	64.9 (55.0, 72.4)	65.3 (55.8, 71.9); 88	66.9 (56.5, 71.4); 41	21.1 (4.1, 52.6); 85	27.0 (6.5, 55.7); 41
Colon	62.7 (47.7, 70.6)	63.1 (48.2, 72.6)	65.2 (48.7, 72.0); 15	71.2 (55.0, 74.3); 9	21.1 (6.9, 24.6); 15	27.3 (3.4, 60.2); 9

Continued

Gastric	66.8 (58.3, 73.6)	71.5 (62.4, 75.0)	71.5 (57.8, 77.9; 10	(66.9, 67.6);2	3.9 (0.5, 30.3); 9	(3.5, 6.0); 2
GI	70.4 (60.1, 78.5)	70.4 (57.5, 77.8)	70.9 (58.1, 77.9; 10	(64.9, 79.4); 2	10.0 (1.2, 23.0); 9	(0.9, 3.9); 2
Pancreas	66.6 (57.2, 69.4)	66.9 (59.0, 72.7)	67.6 (57.4, 73.8); 12	67.2 (59.3, 69.1); 11	4.6 (0.9, 6.9); 11	23.1 (6.9, 27.0); 11
Mamma	48.1 (39.1, 56.9)	58.2 (48.3, 67.6)	58.8 (55.7, 67.7); 15	57.4 (44.3, 64.3); 8	106.1 (42.5, 143.4); 15	102.9 (49.3, 144.5.8); 8
Ovarium	59.9 (51.0, 65.6)	61.9 (54.7, 66.3)	61.0 (54.7, 67.1); 23	(67.8, 75.1); 2	27.9 (19.8, 62.9); 22	(10.6,30.3); 2
Others	62.2 (54.1, 74.7)	63.7 (55.3, 84.0)	(88.0); 1	70.6 (56.2, 75.5); 7	(0.2); 1	29.5 (17.2, 47.6); 7

Data are given as median (1st, 3rd quartile); if only 2 cases were observed minimum and maximum are shown.

found out that the therapy and tolerability improved more the higher Karnofsky-index was, with a cut off of 80%.

Gastrointestinal tumours were often locally advanced with pre-existing PC at diagnosis. Here, the prognosis was worse.

Patients with gynaecologic tumours and PC showed longer survival. PC develops late in the course of disease in mammary CA sometimes 15 years later. The course in the presence of PC, especially in younger women was shown to be very aggressive.

There was no significant difference in age between cancer entities or patients suffering from PC as shown in Table 2. Also, at entry to the PC working group, patients did not differ in age. The time between the initial cancer diagnosis and the entry to the PC working group was similar between patients with and without PC indicating a similar medical history with regard to standard therapy prior entering the PC working group.

3.1. Overall Survival

Deaths occurred due to cardiac or age-specific impairments but not under laparoscopy or systemic and local CTh, so that an evaluation of the previous illnesses (e.g. absolute arrhythmia) seems to be always necessary. However, these data are not fully substantiated in the current observation and would need to be further investigated in clinical trials.

Overall, 95 out of the 132 patients died (72.0%). Median survival in the whole population group was 3.74 years (95% CI, 2.57 to 4.91). Overall survival de-

pended on the cancer entity and was shortest for those suffering from pancreas cancer and PC and highest for patients with mamma carcinoma without PC (as shown in Table 3). However, patients with mamma carcinoma have a shortened lifespan when they develop PC. This needs further studies. After PC diagnosis, however, median survival time was longest for those with ovarian carcinomas (Table 3, Figure 3 and Figure 4).

As shown in Figure 5 Median survival time after inclusion to the working group was longer for patients without PC (16.6 (6.4 - 26.8) months) compared to patients with PC (7.5 (4.4 - 10.6); p-value = 0.155).

In order to assess the possible success of the Lotus Care Cure Program and despite the lack of a control group, it was investigated whether the survival time differs depending on the length of stay in the working group (as a measure of the duration of Lotus Care Cure Program). In addition, the logrank test showed that

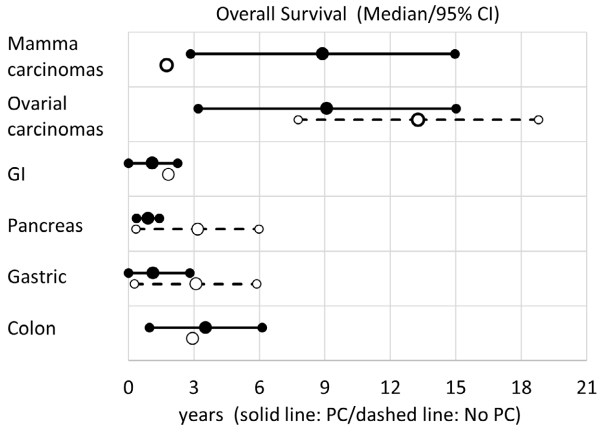

Figure 3. Overall survival analysis in different subgroups after initial diagnosis by entities. Data are given as median survival time (95% CI).

Table 3. Mortality in different subgroups after initial diagnosis by entities.

	Mortality (n; %)	
Male	35; 76.1	
Female	60; 70.0	
Entity	**PC**	**No PC**
All (n = 132)	68; 76.4	27; 62.8*
Colon (n = 24)	13; 85.7	4; 44.4
Gastric (n = 13)	8; 80	2; 66.7
Pancreas (n = 23)	11; 91.7	8; 72.7
GI (n = 12)	9; 90	2; 100
Ovarian carcinomas (n = 25)	13; 56.5	2; 100
Mamma carcinomas (n = 23)	12; 80.0	5; 62.5

*$p_{Logrank} < 0.05$.

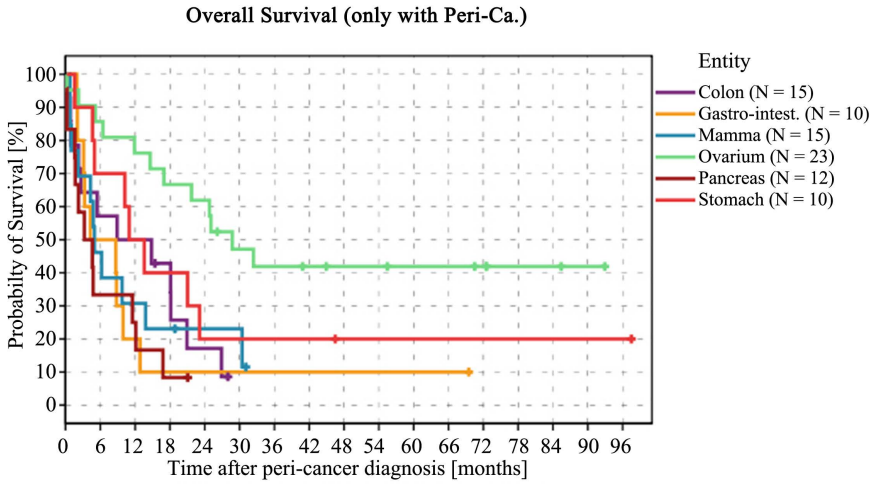

Figure 4. Kaplan-Meier survival time curve according to cancer entities after PC diagnosis (p = 0.004).

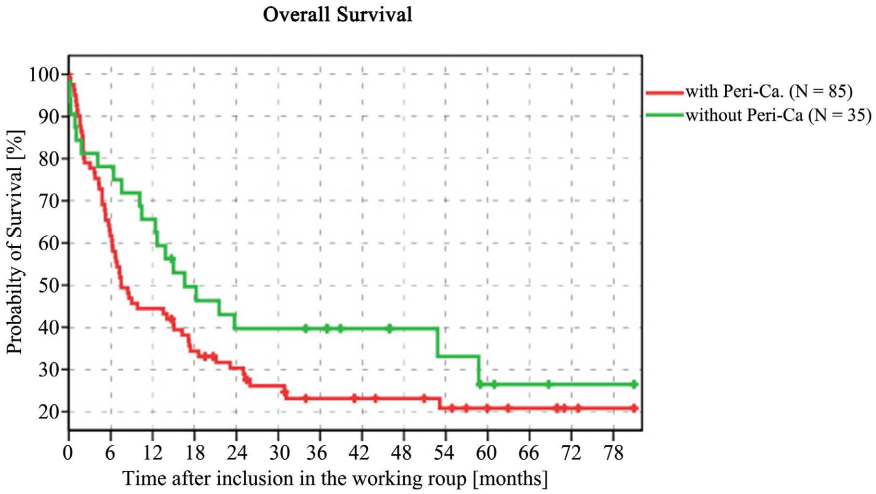

Figure 5. Kaplan-Meier survival time curve after inclusion to the working group in patients with and without PC (p = 0.155).

the survival rates between the entities GI, pancreas and stomach or between breast and ovary carcinoma did not differ significantly (data not shown). Therefore, the respective entities were combined into one group each.

For patients with the combined entities gastric, GI and pancreas cancer, the length of stay in the working group had a significant impact on survival time (shown in Table 4). For patients with the entities gastric, GI and pancreas cancer, the length of stay in the working group had a significant influence on survival time. For the combined entities ovarium and mamma carcinoma, treatment duration was only significantly affecting median survival time in patients with PC but not in those without PC.

3.2. Quality of Life

The self-reported quality of life as well as the domains emotional, social, role,

Table 4. Median survival time (95% CI) of combined cancer entities by lengths of stay to the working group (WG) "Peritoneal-karzinose".

		Magen/GI/Pancreas					
		n	**Entry to WG after initial diagnosis (mean time (±SD) in yr)**	**Mean age (±SD) at initial diagnosis (yr)**	**Karnofsy Index**	**Mean (±SD) duration in WG (yr)**	**Median survival time, yr (95% CI)**
PC	>1 yr in WG	11	1.09 ± 1.64 (0.54)	59.7 ± 16.7 (54.3)*	84.0 ± 8.9	2.38 ± 1.66	1.92 (0.83 - 3.02)
	<1 yr in WG	29	1.12 ± 1.88 (0.54)	65.3 ± 12.3 (66.9)	75.6 ± 10.4	0.34 ± 0.30	0.75 (0.52 - 0.99)**
No PC	>1 yr in WG	13	1.75 ± 1.87 (1.71)	58.9 ± 66.1 (60.7)	82.9 ± 7.6	2.79 ± 1.42	>2.79 (-)
	<1 yr in WG	10	2.60 ± 5.34 (0.67)	66.1 ± 12.6 (67.8)	79.3 ± 8.8	0.33 ± 0.34	1.33 (1.33)**
		Mamma/Ovarium					
PC	>1 yr in WG	22	5.02 ± 5.19 (2.90)	57.4 ± 12.2 (56.5)	85.7 ± 10.8	3.04 ± 1.59	21.79 (7.44 - 36.14)
	<1 yr in WG	17	6.01 ± 6.76 (4.06)	55.6 ± 13.8 (55.7)	79.3 ± 8.8	0.32 ± 0.23	3.46 (0.23 - 6.70)**
No PC	>1 yr in WG	6	6.36 ± 4.32 (6.17)	56.8 ± 14.1 (53.4)	83.3 ± 11.5	2.29 ± 1.55	14.00 (-)
	<1 yr in WG	4	11.12 ± 13.77 (6.21)	42.4 ± 17.9 (38.6)	76.7 ± 5.8	0.42 ± 0.45	3.70 (0.00 - 11.25)

*Significantly different between < or >1 year in WG (t-test), **$p_{Logrank} < 0.05$, Kaplan-Meier analysis.

physical and cognitive functioning decreased in the first 8 weeks of Lotus Care Cure Program and then improved again slightly by week 16 as shown in Figure 6(a) and Figure 6(b). The symptoms scales fatigue, pain and nausea/vomiting showed a similar course. Loss of physical function such as nausea, vomiting or pain was perceived as less serious than lack of professional and/or social integration and money worries.

4. Discussion

The diagnosis of PC, with the exception of primary PC, already represents an advanced tumour disease in stage WHO IV. Survival times of only few months depending on the cancer entity are described in the literature [1] [2] [3]. Previous concepts have not yet been established, presumably as a result of the difficulties in the feasibility of the methods [31].

It was important for the working group to understand PC not only in terms of the TNM system but also in terms of prognostic factors. The function of the peritoneum is also based on intracellular structures that lead to the resorption of fluid and organic substances [32]. Based on this understanding, the peritoneum must possess both hydrophilic and lipophilic transport mechanisms for resorption. The application of systemic CTh usually involves the administration of hydrophilic substances. The PIPAC method also uses hydrophilic doxorubicin. Assuming existing transport mechanisms for absorption and subsequent elimination of lipophilic substances, systemic CTh with use of a lipophilic doxorubicin (here Caelyx) intraperitoneal was always performed after laparoscopically established histopathological diagnosis [31] [33] [34].

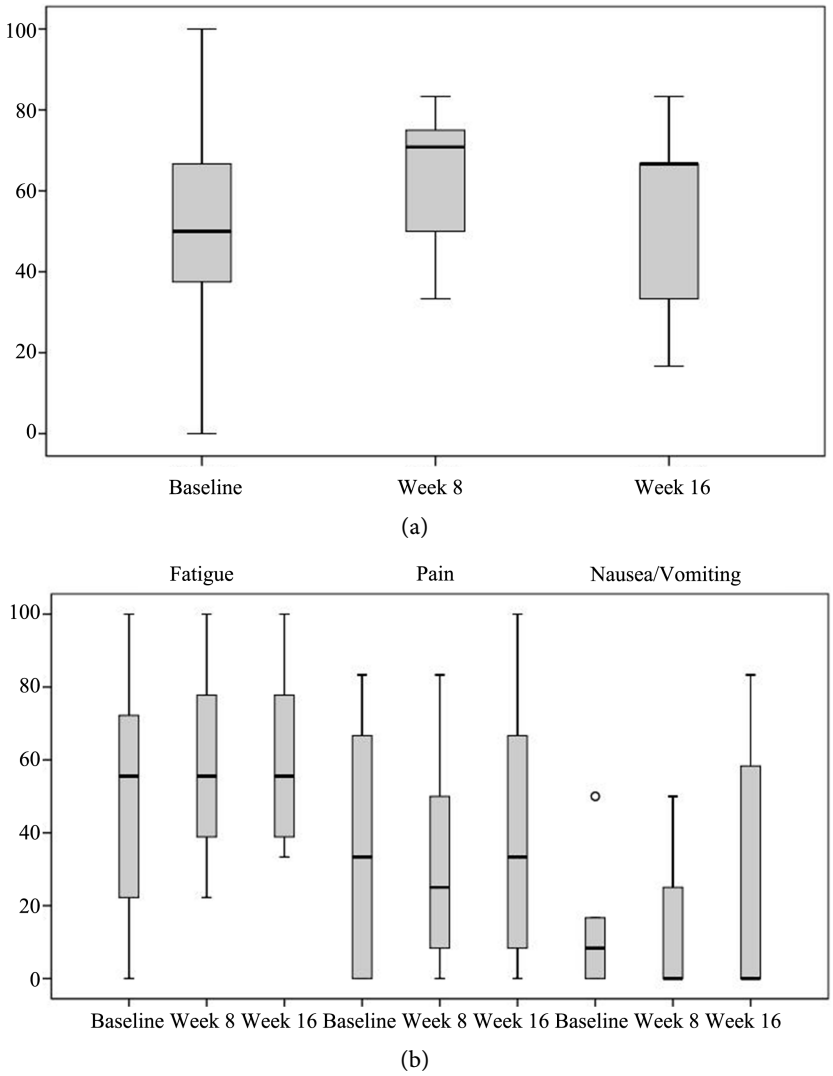

Figure 6. EORTC Global score (a) and symptom scales (b) at baseline, after 8 weeks and after 16 weeks (n = 12). Data are given as median (1st, 3rd quartile); for n = 12 subjects EORTC QLQ-C30 scores are available for all timepoints.

132 patients were included in the working group regardless of age, sex or tumour entity. Histopathological examination of all conspicuous peritoneal foci surprisingly showed no agreement with macroscopic assessment in 32.5% of the cases. Therefore, it can be postulated that accurate histopathologic examination in combination with PCI indication is mandatory for accurate therapy evaluation and should be implemented in the relevant guideline.

The methodology described above is well feasible in everyday life under both inpatient and outpatient conditions. Therapy discontinuations or deaths were not directly related to the therapy measure, but were dependent on therapy-relevant pre-existing conditions. In this respect, an evaluation of the previous diseases with regular monitoring of these during the therapy measures is necessary. The majority of deaths occurred in the first 16 weeks. In the subsequent period, a clear survival of the patients could be observed. Patient survival in the present

observation was up to 33 months in some cases. This should be urgently confirmed in further clinical studies.

Second look laparoscopy was performed for response assessment and further therapy evaluation. In case of reduction of PCI, the Ki67 changed, as already described for other tumour diseases. In case of a good response, the further therapy strategy was continued systemically according to the relevant guidelines. Local i.p. therapy included only abdominal lavage with regular cytological examination of the installation fluid.

The working group observed that as a result of downstaging and downsizing other therapy concepts with (conditionally) curative intention, such as the modified Sugarbacker surgery or hyperthermia become possible.

Quality of life was most impaired between weeks 8 and 16, with patients feeling impaired not because of pain or symptoms, but because of limited social contacts and/or occupational inactivity or financial fears.

4.1. Summary

The diagnosis and therapy of PC requires a multi-professional team of therapists and a multimodal therapy concept jointly decided in a tumour conference. The multimodal concept together with the Lotus Care Cure project shows very good feasibility with high compliance and ultimately leads to better and low-risk patient care. Prior to a planned therapy, a precise histopathological examination of the peritoneal foci with indication of PCl, review of histology, Ki67 and further immunohistochemical information is necessary to avoid false negative or positive statements. The Karnofsky index as well as the calculation of organ reserves provides information about the feasibility of subsequent both systemic and local CTh and the expected side effects. In addition to the previously evaluated organ reserves, it is important to monitor pre-existing conditions throughout the duration of the therapeutic intervention as well as standardized regular adherence to pain management prior to initiation of intraperitoneal CTh installation. The combination of systemic with local CTh leads to a better therapy response, as other research groups have also demonstrated [35] [36]. If tumour debulking in the sense of downstaging and/or downsizing is successful, other therapy concepts with (conditionally) curative intention should be evaluated. In addition, with the additional implementation of the complementary LOTUS Care Cure Project, the quality of life of patients can be improved. A suggested flow chart can be found in **Figure 7**, which was developed by the working group in 2018/2019.

4.2. Outlook

The peritoneum is not an appendage, but an organ. Therefore, understanding the tumour biology of peritoneal carcinomatosis is important for the application of the correct therapeutic measure in order to be able to guarantee an individualized procedure.

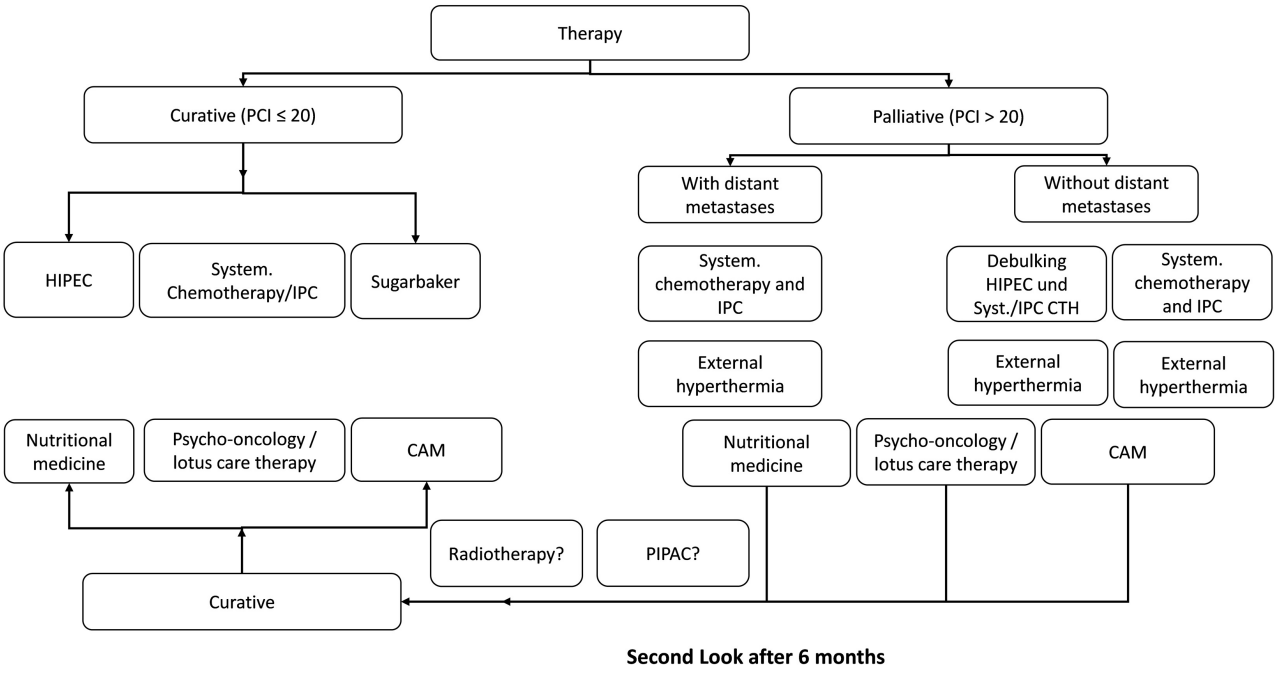

Figure 7. Suggestions for a PC therapy process.

Histopathological characterization of peritoneal carcinomatosis is therefore of particular importance. Further studies are needed to verify the feasibility and the results also in other centres.

In some cases, the method could lead to downstaging and downsizing. It should be examined to what extent other therapy concepts such as modified Sugarbaker surgery, stereotaxi and hyperthermia bring a positive contribution to further survival benefit.

Thus, an extremely palliative disease could be curative in individual cases with a palliative therapeutic approach as shown in **Figure 7**. The results encourage not to give up the efforts for the treatment of peritoneal carcinomatosis and to search for new ways and possibilities. There is a great need for a standardized and multimodal treatment guideline for PC and that complementary approaches such as LOTUS Care Cure should be more widely applied to mitigate the side effects of chemotherapy and thus improve quality of life.

4.3. Vision

"I have a dream" (from Doctor Martin Luther King, 1963), peritoneal carcinomatosis will possibly become in future a treatable and even curable disease.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

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