ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 09 | September - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

RETROSPECTIVE ANALYSIS OF OVERALL SURVIVAL FOLLOWING CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) FOR PERITONEAL MALIGNANCIES: A SYSTEMATIC REVIEW.

Oncology

Uma Sharma
MS Ganesh
CM Giridhar

ABSTRACT

Peritoneal malignancies (PM) are caused by the intravascular distribution of tumors from a number of primary histopathological illnesses, and patients frequently die less than a year after diagnosis as a result of intestinal obstruction. Patients with PM are now more frequently handled with hyperthermic intraoperative chemotherapy (HIPEC) treatment following the Cytoreductive surgery (CRS). This systematic analysis intends to retrospectively analyze the overall survival outcomes linked to CRS and HIPEC in managing different peritoneal cancers. A thorough literature search using several internet sources turned out 14 studies that were suitable that were published between 2007 and 2023. These investigations included a wide variety of peritoneal malignancies, such as appendiceal neoplasms, colorectal cancer, ovarian cancer, and mesothelioma. The patient's median survival time ranged between 30.1 and 85 months. The median disease-free survival (DFS) ranged from 8.2 to 30 months, while survival at five years ranged from 14% to 57.8%. Different malignancy types showed diverse survival results in subgroup analysis, with appendiceal neoplasms and colorectal cancer showing comparably greater survival rates. The observed increase in overall survival emphasizes the possible advantages of this therapeutic strategy, especially for patients with appendiceal neoplasms and intestinal cancer.

KEYWORDS

Hyperthermic Intraperitoneal Chemotherapy, Cytoreductive surgery, systematic review, Peritoneal Malignancies, inclusion criteria, survival outcome.

INTRODUCTION

Intracavitary tumor spreading from an array of initial histopathological abnormalities causes peritoneal malignancies, and sufferers frequently die within a year or less of their diagnosis due to bowel obstruction [1]. Colorectal and appendiceal cancers, as well as ovarian mesothelioma, sarcomas, and, carcinomas are among the gastrointestinal cancers that frequently exhibit such features. However, Sugarbaker recognized localized chemotherapy and surgical removal of a macroscopic tumor as a workable alternative therapy [2]. Since that time, CRS in conjunction with HIPEC has become more widely employed to treat peritoneal surface cancer patients. For CRS/HIPEC as a therapeutic option for PM within the last 20 years, an increasing collection of evidence has emerged. As a result, more clinics have started using this modality, which has helped this procedure's popularity grow exponentially.

To boost the effectiveness and potency of the anti-neoplastic drugs, hyperthermia was also increasingly used in the 1970s and 1980s in conjunction with intraperitoneal chemotherapy [3]. The combination of HIPEC and CRS has subsequently been recognized as a critical method for managing peritoneal illness and has been linked to improved survival rates in a subset of patients [4]. The outcome is influenced by a variety of variables, including the initial tumor's subtype, the peritoneal cancer index (PCI)-determined extent of carcinomatosis, and the degree of radicality of the operation. With this cutting-edge treatment plan, the goal is to manage the dangers that come with major surgery and intensive chemotherapy while also extending patients' lives. A thorough examination of its results is essential as the medical community strives to improve and broaden the application of CRS and HIPEC.

Growing clinical experiences and retrospective investigations have served as the foundation for the development of CRS-HIPEC. Although various single-center and multicentre trials have shown encouraging survival results, the efficacy of CRS-HIPEC is still up for question because there are differences in patient selection, surgical methods, chemotherapy regimens, and study design. To give a more thorough evaluation of the overall survival advantages reaped from this therapeutic approach across various peritoneal cancers, a thorough systematic analysis is necessary. This review seeks to give clinicians, researchers, and policymakers a thorough understanding of the emerging landscape of CRS-HIPEC by synthesizing the available evidence and illuminating trends, disparities, and prognostic factors.

Search Strategy

According to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards", this systematic review was carried out. To search Science direct, PubMed, BMC, Embase, Medline, and the Cochrane collaborative library, the medical subject headings "cytoreductive surgery" and "hyperthermic intraperitoneal chemotherapy" were used.

Inclusion Criteria

We only took into account full-text English publications published between 2007 and 2023 that provided information on life expectancy outcomes after "CRS and HIPEC". Studies exploring the outcomes via retrospective studies were only considered for further selection criteria. Using thorough cross-referencing using the citations of the publications in the initial search, further papers that had not yet been discovered were included.

Exclusion Criteria

Studies that did not conduct a follow-up analysis following therapy were disregarded. Studies that reported on various malignancies were evaluated, and those that could not extract PCI data unique to PM were eliminated. Clinical trial studies and other studies other than retrospective cohort studies were excluded. Additionally disregarded were analyses based on a single subject. Studies that were abstracted and had poor or nonexistent perioperative or survival results were also removed and studies focused only on complications were also eliminated.

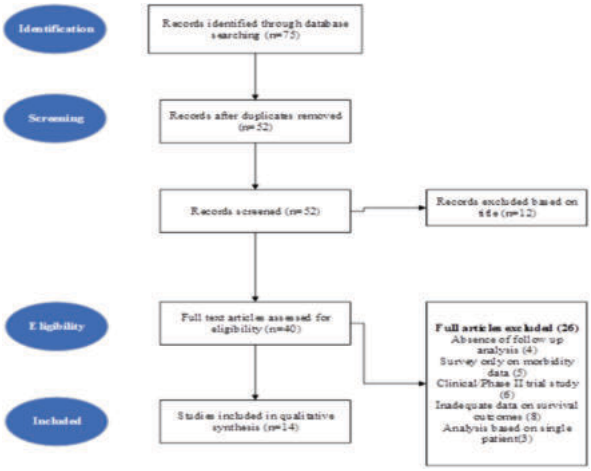

Figure 1: Flowchart Demonstrating The Identification Of Relevant Studies.

RESULTS

Choice of studies

Figure 1 depicts the procedure for choosing and screening the studies that would be included in this evaluation. The final analysis contained

14 studies that met the criteria. They were all retrospective cohort designs.

Procedures For Using CRS/HIPEC

CRS was based on the Sugarbaker, and all trials documented the surgery and chemotherapeutic methods. The variability of the HIPEC regimen utilized in these studies is a challenge when evaluating the findings for colorectal peritoneal metastases. These include the HIPEC procedure, the chemotherapeutic medications utilized, the dosage, the length of the procedure, and the HIPEC temperature.

Outcomes After CRS and HIPEC

Overall survival was discussed in all 14 trials. The patients in this group had an average time to death of 30.1 to 85 months [6-8,10-13,15,17,18]. Survival at five years varied from 14% to 57.8% [5,8-14,17,18]. The range of the median time without illness (DFS) was 8.2 to 30 months [7,8,10-13,15,16,18].

Mortality And Morbidity

The mortality and morbidity rates for grade 3/4 were reported and the death rates ranged from 0 to 4.2%, while major morbidity ranged from 15.1% to 56%.

DISCUSSION

Treatment Procedures Implemented In The Reviewed Studies

The CRS procedure, as outlined by Sugarbaker, focuses on the comprehensive removal of macroscopic peritoneal disease [5-18]. Following CRS, HIPEC is employed to target microscopic disease, particularly lesions smaller than 3 mm [5-18]. In several investigations, HIPEC was utilized only when there was a (near) 100% cytoreduction [15]. However, within the same tumor histopathology group, the medication given (Mitomycin C), the length of the HIPEC, and the ambient temperature at which it was given stayed the same throughout all of the investigations. The chemotherapeutic drugs utilized for the HIPEC varied depending on the location of the main tumor. The prescription of chemicals for chemotherapy has differed in studies indicating different procedures followed in respective institutions.

Table 1: Details Of Reviewed Studies.

Study ID	Author	Year	Study design	Year of survival	No of patients	Patient age group	Drugs
5	Teo *et al*.	2013	Retrospective Observational Study	2001-2012	100	51.5 (14-74)	Mitomycin C, Cisplatin
6	Sutton *et al*	2021	Retrospective Cohort Study	2003-2019	1259	51.3 (44-65)	Mitomycin C, Oxaliplatin, folinic acid, 5-fluorouracil
7	Assaf *et al*.	2022	retrospective analysis	2015-2020	280	59 (21.5-87)	Mitomycin, Fluorouracil, leucovorin
8	Passot *et al*	2016	Retrospective Observational Study	1989-2015	1125	56 (17-81)	Cisplatin, Mitomycin C, Oxaliplatin, Doxorubicin, and Irinotecan
9	Kusamura *et al*	2021	retrospective analysis	1993-2017	1924	54 (44-63)	mitomycin C, oxaliplatin, doxorubicin, and irinotecan
10	Giorgio *et al*.	2016	Retrospective Multicenter Study	1998-2014	511	57.1 (29-75)	mitomycin C, oxaliplatin, doxorubicin, and irinotecan
11	Giorgio *et al*.	2008	Retrospective study	2000-2007	47	60.3(32-75)	Neoadjuvant chemotherapy with paclitaxel and cisplatin
12	Narasimhan *et al*	2019	Retrospective cohort study	2009-2018	333	56 (47-66)	mitomycin C, oxaliplatin, doxorubicin, and irinotecan
13	Baratti *et al*	2018	retrospective cohort study	2004-2016	148	59(51-65.5)	mitomycin C/cisplatin
14	Kamada *et al*	2021	retrospective descriptive study	1990-2015	236	59 (24-80)	"Fluorinated pyrimidine plus oxaliplatin or irinotecan, ± bevacizumab or panitumumab, cisplatin plus mitomycin C"
15	Hentzen *et al*.	2019	Retrospective Observational Study	2006-2017	433	64(NR)	Mitomycin C
16	Chia *et al*	2016	Retrospective study	2012-2015	23	52 (25-71)	Mitomycin C
17	Elias *et al*	2010	Retrospective cohort study	1990-2007	523	54(16-88)	Mitomycin C, Oxaliplatin, irinotecan
18	FRØYSNES *et al*	2016	Retrospective study	2004-2013	119	58(22-77)	Mitomycin C

Survival Outcomes

The significance of the PCI score and the CC score and their influence on the outcomes of survival in patients undergoing CRS and HIPEC were assessed in a systematic review encompassing numerous articles. The study emphasized the critical significance of obtaining optimal cytoreduction (CC 0/1); no discernible longevity benefit compared to conventional treatment was seen among individuals with CC grades of 2 and 3. The research found a subtle difference between cancer patients' overall survival or disease-free survival after "CRS and HIPEC". The studies employed the "Kaplan-Meier method" to determine survival indices for "Overall Survival (OS) and Disease-Free Survival (DFS)" [5-18]. A notable survival rate of 91.7% after 1 year fell to 50.9% after 5 years among 100 carefully chosen patients in Asian nations with peritoneal carcinomatosis. It's interesting to note that some survivors' illness predominance maintained even after therapy, with only a small 26.3% obtaining disease-free survival at the

5-year milestone [5].

A different experiment including ovarian cancer patients found that the disease-free survival rate was 15.2%, much lower than the overall survival rate, which was 60.7% after five years. 90% of patients achieved CC scores of 0, 7% achieved CC-1, and CC 2/3/4 was seen among 3%. Attaining CC 0/1 was revealed to be a crucial component that significantly influenced both DFS and OS [5–18]. The review additionally supported the idea of repeat CRS/HIPEC for patients with recurrent disease amenable to such treatment, as demonstrated by successful outcomes. A comparison showed that first advanced cancer required more surgical procedures than recurring ovarian cancer, with the latter having a better Progression-Free Survival (PFS) rate.

Given the extremely positive outcomes in this group, depending on the magnitude and spread of the disease, patients with PMP who are prone to CRS/HIPEC ought to be assessed for recurrent operation. Repeat CRS/HIPEC is safe, has a median survival of more than 6 years, and instant consequences such as duration of residence, general problems, and complex issues are similarity among index and follow-up procedures. 89% of patients with appendix cancer, 74% of patients with PMP, and 86% of patients with CRPM experienced complete (CC0/1) cytoreduction [6]. It's interesting to note that the pattern of peritoneal colorectal metastatic distribution was a key factor in determining the survival rates following CRS/HIPEC. In instances with dispersed metastases, the average duration of disease-free survival was 8.2 months, but in those with clustering metastases, it was 22.5 months [7], and SPS patients have worse OS and DFS regardless of PCI level. Scattered metastases were also associated with worse OS. Chemotherapy was proven to be an essential supplementary therapy after CRS, resulting in higher overall survival rates. Different HIPEC regimens, such as oxaliplatin plus fluorouracil-leucovorin and cisplatin plus mitomycin, showed variable prognostic benefits. The median peritoneal cancer index declined year over year, and fewer patients experienced partial cytoreduction, according to a study from Lyon Sud Hospital in France, which involved executing 1125 HIPEC procedures over 25 years. Significantly fewer people died (from 5% to 2%). Mesothelioma, gastric PC, ovarian, colorectal, and Pseudomyxoma had recurrence-free survival rates after 10 years of 14%, 9%, 4%, 10%, and 53% respectively, while the median overall survival was 42 months [8]. In the Kamada *et al*. trial, 14.0% of patients survived long-term, meaning for more than five years. Extended survivors' median PCI was lesser than that of non-survivors'. CCR-0 was experienced by all enduring survivors, and it happened substantially more frequently [14].

While optimal cytoreduction was related to a Peritoneal Cancer Index below 15, a higher index did not always rule out positive surgical results. Notably, survival rates were dramatically increased with macroscopically whole resections (CC 0/1). Primary cancer type was found to be a significant influence in OS, with patients with peritoneal, mesothelioma, appendiceal, and ovarian cancer having higher survival rates than those with colorectal cancer. Ovarian tumour chemosensitivity played a role in the improved OS in this subgroup. The systematic review's conclusion highlighted the complex interaction between some variables, including the CC score, PCI score, metastatic distribution pattern, and the underlying cancer type, in determining the survival results of individuals receiving both "CRS and HIPEC". In the research by Kusamura *et al*, the significance of chemotherapy following CRS was well-documented. The CRS-HIPEC group demonstrated improved Rates of survival over five years compared to the CRS-alone group for various categories, including better survival rates and improved percentage showing a Cytoreductive score of 0/1. Additionally, the HIPEC regimens with "cisplatin + mitomycin and oxaliplatin" showed a greater prognosis improvement [9].

With regard to those who have ovarian cancer recurrence, people with primary advanced cancer required more surgical operations. Patients with primary metastatic ovarian cancer had a tendency towards a greater OS comparison to those who had resurgence treatment, but a noticeably better PFS. A substantial difference in OS and PFS was seen between main metastatic ovarian cancer patients who received CRS and HIPEC, according to outcome analyses [10]. Research by Giorgio *et al*. found that the mainstream of patients (95.6%) had a good performance level at discharge and that the average 5-year survival rate was 16.7%, the DFS was 27.4 months, and the overall survival was 30.4 months on average. Peritonectomy combined with HIPEC appears to be justifiable for both primary and secondary cytoreduction, which was previously only reserved for "secondary cytoreduction patients", because it was only thought of as a last resort for those with "recurring or chemotherapy-resistant ovarian cancer". Even if a PCI below 15 is a deciding aspect of achieving appropriate cytoreduction, a PCI above 15 may not always rule out obtaining outstanding surgical results [11].

In comparison to the first group, the subsequent cohort had a significantly greater number of macroscopically entire resections (CC 0/1). This was further demonstrated by a greater number of CC 0/1 resections in PMP and CRPM instances in the subsequent cohort in comparison with the first cohort, "a median OS of 85 months, a 5-year survival rate of 52%, and a median DFS of 30 months with a 5-year survival rate of 37%", reported in a retrospective evaluation of 384 cases, respectively [12]. There was also no apparent improvement in OS after the subsequent cohort, though a "3-year existence rate of 65%". Patients with no postoperative, low-grade, or high-grade problems had improved 5-year OS rates, with an overall survival rate of 43%. Patients with primary peritoneal cancer, appendiceal PC, and ovarian PC other cancers all fared much better than those with colorectal PC in terms of survival. The average survival time of patients with PCI 8 and EPD was 27.0 months when assessing the prognostic value of the presence of extraperitoneal disease that had been successfully treated simultaneously with or preceding the occurrence of peritoneal metastases [13]. According to research by Chia *et al*., "the median DFS rate for the 23 patients was 12.9 months, and the 3-year overall survival rate was 77.4%". Recurrences occurred in two patients after three months, five after six months, and seven after a year [16]. The lengthier surgery and higher PCI could indicate a more involved procedure with a longer recovery time. Unfortunately, having a stoma was linked to both a lower quality of life and an increased risk of an early recurrence.

A significant association exists between the PCI, the degree of CRS completion, as well as morbidity and death. The 5-year survival rate is less than 10% when the PCI is higher than 20, demonstrating that a relative restriction to this combination therapy is a severe illness [17]. Primary cancer and CC score on the log-rank test were factors impacting OS [5]. The OS was impacted by the main tumor, with colorectal patients faring worse than those with primary ovarian, appendiceal, peritoneal, and mesothelioma cancers. This could improve OS in these patients in addition to tumor biology. Due to this category of tumours' exceptional chemosensitivity, ovarian patients' OS has improved. The vast majority of those who were disease-free after 2 years continued to be so, while those who had relapsed illness preferred to do so early—that is, inside the first 2 years. This is probably due to the locoregional disease-like behavior of PC, which causes instances of recurring to frequently arise at early phases. Disease-free status at the 2-year term indicates favorable OS and DFS [5].

Table 2: Survival Of Patients Treated With CRS And HIPEC.

Study ID	Median OS %			Median OS month	Median CC 0/1 obtained (%)	Median DFS %			Median DFS month
	1st year	3 rd year	5th year			1st year	3rd year	5th year	
5	91.7	59.1	50.9	NR	NR	61.4	32.9	26.3	NR
6	NR	NR	NR	62.6	96.8	NR	NR	NR	NR
7	NR	NR	NR	35.7	NR	NR	NR	NR	8.2
8	NR	NR	42.5	42	NR	NR	NR	27.6	17.25
9	NR	NR	57.8	NR	77.40%	NR	NR	NR	NR
10	NR	NR	44.4	52.4	72.6	NR	NR	25.2	16.6
11	NR	NR	16.7	30.4	87.3	NR	NR	NR	27.4
12	NR	NR	52	85	82.3	NR	NR	NR	30

13	NR	NR	47.8	35.6	NR	NR	NR	22.9	11.5
14	NR	NR	14	NR	84.9	NR	NR	6.8	NR
15	NR	NR	NR	34	99	NR	NR	NR	13
16	NR	77.4	NR	NR	96	NR	NR	NR	12.9
17	81	41	27	30.1	84	47	15	10	NR
18	NR	65	36	47	NR	NR	NR	14	10

Postoperative Complications

The probability of experiencing postoperative problems was found to increase by 53% for every successive resection procedure. Respiratory problems and intra-abdominal collections were the main issues with this high-grade category of sequelae. A total of 55 individuals were involved, and 45 of them had severe problems (rated from 3 to 5) [5]. Patients' conditions differed significantly from one another with higher intraoperative blood loss and those with lower blood loss in terms of their tendency for high-grade problems (recurrence rate after full cytoreduction was 26.4%, with 25.5% of patients requiring repeat surgery) [6].

Patients with peritoneal carcinomatosis have exhibited increased survival rates when CRS and HIPEC were combined. The choice of chemotherapeutic drugs, however, affects morbidity. Preoperative renal function optimization, individualized chemotherapy regimens, vigilant monitoring of renal function markers, and cautious fluid management throughout and following surgery were all used to reduce nephrotoxicity. Intriguingly, postoperative complications were the same in all categories despite differences in survival rates between clustered and scattered kinds of peritoneal carcinomatosis. Only one of the 280 patients that were surveyed had a fatal outcome [7]. It should be noted that the CC-2/3 subgroup showed reduced HIPEC efficacy as a result of difficulties with medication penetration within significant residual illness [9]. The reasons of postoperative death were "sepsis resulting from stomach necrosis, septic shock leading to multiorgan failure, pulmonary failure and acute respiratory distress syndrome (ARDS), and liver failure" [5-18].

Even with normal preventive efforts, pleural effusion, and wound infection were found to constitute a considerable danger, helping to contribute to a 4.2% in-hospital mortality rate. Treatment-related difficulties were brought on by the use of loco-regional chemotherapy, particularly issues connected to prolonged drug delivery and catheter installation through the abdominal wall [11]. "Deep vein thrombosis and subacute intestinal obstruction (SAIO)" were the two most prevalent severe morbidities, and "sepsis, burst abdomen, lymphocele, neutropenia, urinoma, acute renal failure, and enterocutaneous fistula" were also prevalent [11].

Complete excision was frequently only possible with diaphragmatic surgery during CRS in conjunction with HIPEC. It was connected, nonetheless, to increased postoperative morbidity, notably haemorrhage. Up to two organ resections were necessary in a sizable percentage of cases, and more severe multi-organ resections were necessary in one in five instances. Percutaneous drainage was typically used to treat cases of intra-abdominal accumulation. Although renal failure requiring renal replacement treatment was uncommon, three perioperative deaths were reported in the retrospective investigation out of 384 cases [12]. Regardless of whether EPD treatment started before PM onset or happened concurrently with CRS/HIPEC, patients who were treated for extra-peritoneal disease (EPD) as well as peritoneal metastases (PM) had lower overall survival rates than those who were only treated for PM. This decline in survival was linked to the ability of tumors with PM and EPD to disseminate through several pathways [13]. Notably, a greater rate of operational death was observed in patients who had liver resections along with CRS/HIPEC [13].

Despite the postoperative complication in patients after CRS/HIPEC, the level of mortality is very low comparing the survival rates and still patients survived with meagre complications. Some studies revealed the improvement in Cytoreduction score after performing repeated surgery and thus improving the survival period.

Table 3: Morbidity And Mortality Of Patients Treated With CRS And HIPEC

Study ID	Median PCI score	Median follow up	Major morbidity %	Mortality %
5	13	21	56%	0
6	16	22.7	NR	NR
7	7	15.27	NR	0.65
8	NR	31	50%	2
9	NR	52	32	2.1
10	12.7	53.8	25.4	NR
11	14.9	NR	21.3	4.2
12	11	24	26.3	0.8
13	10	34.6	27.7	3.4
14	9	NR	26.2	NR
15	8	NR	22.5	1.6
16	8	18.5	24	0
17	NR	45	31	3.3
18	NR	45	15	NR

CONCLUSION

For the management of CRPM, CRS and HIPEC in amalgamation with systemic contemporary chemotherapy routines is safe and practical. Since its introduction under Sugarbaker, the use of "CRS and HIPEC" has grown dramatically. Referrals of CRPM patients to skilled facilities that can provide specialized, interdisciplinary examination and top-notch surgery are crucial. Additional evidence points to the improvement of OS and DFS with CRS and HIPEC. Personalized therapies driven by the application of patient-derived tumoroids are currently revealing fresh and off-label chemotherapeutic approaches to increase lifespan for those with this fatal form of colon cancer.

REFERENCES

[1]. Levine, E.A., Stewart IV, J.H., Shen, P., Russell, G.B., Loggie, B.L. and Votanopoulos, K.I., 2014. Intraperitoneal chemotherapy for peritoneal surface malignancy: experience with 1,000 patients. *Journal of the American College of Surgeons*, *218*(4), pp.573-585.

[2]. Sugarbaker, P.H., 2012. Cytoreductive surgery plus hyperthermic perioperative chemotherapy for selected patients with peritoneal metastases from colorectal cancer: a new standard of care or an experimental approach?. *Gastroenterology research and practice*, *2012*.

[3]. Neuwirth, M.G., Alexander, H.R. and Karakousis, G.C., 2016. Then and now: cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (HIPEC), a historical perspective. *Journal of gastrointestinal oncology*, *7*(1), p.18.

[4]. Foster, J.M., Zhang, C., Rehman, S., Sharma, P. and Alexander, H.R., 2023. The contemporary management of peritoneal metastasis: A journey from the cold past of treatment futility to a warm present and a bright future. *CA: A Cancer Journal for Clinicians*, *73*(1), pp.49-71.

[5]. Teo, M.C.C., Tan, G.H.C., Tham, C.K., Lim, C. and Soo, K.C., 2013. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in Asian patients: 100 consecutive patients in a single institution. *Annals of surgical oncology*, *20*, pp.2968-2974.

[6]. Sutton, P.A., O'Dwyer, S.T., Barriuso, J., Aziz, O., Selvasekar, C.R., Renehan, A.G. and Wilson, M.S., 2021. Indications and outcomes for repeat cytoreductive surgery and heated intra-peritoneal chemotherapy in peritoneal surface malignancy. *Surgical Oncology*, *38*, p.101572.

[7]. Assaf, D., Mor, E., Laks, S., Zohar, N., Benvenisti, H., Hazzan, D., Segev, L., Akopyan, O.K., Shacham-Shmueli, E., Margalit, O. and Halpern, N., 2022. The pattern of peritoneal colorectal metastasis predicts survival after cytoreductive surgery and hyperthermic intra-peritoneal chemotherapy. *European Journal of Surgical Oncology*, *48*(1), pp.197-203.

[8]. Passot, G., Vaudoyer, D., Villeneuve, L., Kepenekian, V., Beaujard, A.C., Bakrin, N., Cotte, E., Gilly, F.N. and Glehen, O., 2016. What made hyperthermic intraperitoneal chemotherapy an effective curative treatment for peritoneal surface malignancy: a 25-year experience with 1,125 procedures. *Journal of surgical oncology*, *113*(7), pp.796-803.

[9]. Kusamura, S., Barretta, F., Yonemura, Y., Sugarbaker, P.H., Moran, B.J., Levine, E.A., Goere, D., Baratti, D., Nizri, E., Morris, D.L. and Glehen, O., 2021. The role of hyperthermic intraperitoneal chemotherapy in pseudomyxoma peritonei after cytoreductive surgery. *JAMA surgery*, *156*(3), pp.e206363-e206363.

[10]. Di Giorgio, A., De Iaco, P., De Simone, M., Garofalo, A., Scambia, G., Pinna, A.D., Verdecchia, G.M., Ansaloni, L., Macrì, A., Cappellini, P. and Ceriani, V., 2017. Cytoreduction (peritonectomy procedures) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) in advanced ovarian cancer: retrospective Italian multicenter observational study of 511 cases. *Annals of surgical oncology*, *24*, pp.914-922.

[11]. Di Giorgio, A., Naticchioni, E., Biacchi, D., Sibio, S., Accarpio, F., Rocco, M., Tarquini, S., Di Seri, M., Ciardi, A., Montruccoli, D. and Sammartino, P., 2008. Cytoreductive surgery (peritonectomy procedures) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) in the treatment of diffuse peritoneal carcinomatosis from ovarian cancer. *Cancer*, *113*(2), pp.315-325.

[12]. Narasimhan, V., Das, A., Warrier, S., Lynch, C., McCormick, J., Tie, J., Michael, M., Ramsay, R. and Heriot, A., 2019. Evaluation of cytoreductive surgery and HIPEC for peritoneal surface malignancies: analysis of 384 consecutive cases. *Langenbeck's Archives of Surgery*, *404*, pp.527-539.

[13]. Baratti, D., Kusamura, S., Iusco, D., Cotsoglou, C., Guaglio, M., Battaglia, L., Virzì, S., Mazzaferro, V. and Deraco, M., 2018. Should a history of extraperitoneal disease be a contraindication to cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for colorectal cancer peritoneal metastases?. *Diseases of the Colon & Rectum*, *61*(9), pp.1026-1034.

[14]. Kamada, Y., Hida, K., Ishibashi, H., Sako, S., Mizumoto, A., Ichinose, M., Padmanabhan, N., Yoshida, S. and Yonemura, Y., 2021. Thirty-three long-term survivors after cytoreductive surgery in patients with peritoneal metastases from colorectal cancer: a retrospective descriptive study. *World Journal of Surgical Oncology*, *19*(1), pp.1-13.

[15]. Hentzen, J.E., Rovers, K.P., Kuipers, H., van der Plas, W.Y., Been, L.B., Hoogwater, F.J.,

van Ginkel, R.J., Hemmer, P.H., van Dam, G.M., de Hingh, I.H. and Kruijff, S., 2019. Impact of synchronous versus metachronous onset of colorectal peritoneal metastases on survival outcomes after cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC): a multicenter, retrospective, observational study. *Annals of surgical oncology*, *26*, pp.2210-2221.

[16]. Chia, C.S., Tan, G.H.C., Lim, C., Soo, K.C. and Teo, M.C.C., 2016. Prospective quality of life study for colorectal cancer patients with peritoneal carcinomatosis undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *Annals of surgical oncology*, *23*, pp.2905-2913.

[17]. Elias, D., Gilly, F., Boutitie, F., Quenet, F., Bereder, J.M., Mansvelt, B., Lorimier, G., Dubè, P. and 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*(1), pp.63-68.

[18]. Frøysnes, I.S., Larsen, S.G., Spasojevic, M., Dueland, S. and Flatmark, K., 2016. Complete cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for colorectal peritoneal metastasis in Norway: prognostic factors and oncologic outcome in a national patient cohort. *Journal of surgical oncology*, *114*(2), pp.222-227.