

## Review Article

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## Colorectal Peritoneal Metastases State of Art

Spiliotis John

Director and Chairman, 4<sup>th</sup> Department of Surgery and Surgical Oncology European Interbalkan Medical Center, Thessaloniki Greece**ABSTRACT**

The presence of peritoneal metastasis (PM) in patients with colorectal cancer (CRC) is associated with an extremely poor prognosis.

Recent developments in the field of treatment including new drugs, translational research for new molecules offer a future plan to achieved improved of Survival.

On the other hand, numerous clinical trials regarding the role of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy have now opened new doors in peritoneal metastasis treatment.

This review presents all the controversial data and options regarding this approach.

**\*Corresponding author**Spiliotis John, Director and Chairman, 4<sup>th</sup> Department of Surgery and Surgical Oncology European Interbalkan Medical center, Thessaloniki Greece.

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**Introduction**

Colorectal cancer is the 3<sup>rd</sup> United States most common cancer diagnosed in the United States [1]. Unfortunately, up to 20% of new CRC cases have metastases at time of diagnosis. The most well-known destinations of metastatic ailment in CRC are the liver, lung, and peritoneum.

The peritoneum is the third most common site of metastases from colorectal cancer but carries the worst overall survival among all sites. Patients with colorectal peritoneal metastases (PM) had a median overall survival of only 5.2 months [2].

The main reasons for this are multifactorial, including variable tumor biology, poor penetration of drugs into peritoneal cavity and tissue and resistance to standard chemotherapeutics and an altered tumor microenvironment.

**Treatment Approach**

One treatment methodology that is aggregating for patients with CRC furthermore, PC is hyperthermia intraperitoneal chemotherapy (HIPEC) joined with cytoreduction medical procedure CRS. One of numerous difficulties of treating PC in stage IV CRC patients is tranquilizing conveyance. It is regularly hard to accomplish satisfactory medication levels inside the peritoneum. In the event that chemotherapy portions are along these lines expanded in endeavors to raise tranquilizes fixations the patient is presented to increasingly foundational reactions. HIPEC expects to convey chemotherapy legitimately to the peritoneum, which can build nearby medication concentrations, just as diminish the absolute fundamental introduction from the chemotherapy.

HIPEC is typically preceded by CRS. CRS helps with expelling to such an extent, so that HIPEC can have the best local exposure possible. The patient must be thoroughly assessed for CRS, the

same number of patients may not be possibility for medical procedure. Potential contraindications to CRS incorporate broad intra-stomach lymph hub metastases and broad little inside inclusion. In addition to PC, numerous patients with earlier intrastomach careful history may have attachments that can be cleared to help increment chemotherapy introduction. HIPEC can be regulated legitimately into the peritoneal depression after CRS.

As CRS and HIPEC are still accumulating data, there are a set number of clinical preliminaries off which to base regimens. One study showed a median overall survival of 19.2 months in patients treated with CRS and HIPEC [3,4]. The general survival was expanded to roughly 32 months when there was finished CRS. Another examination exhibited an overall middle survival advantage when looking at CRS and HIPEC (22.3 months) to palliative medical procedure joined with fundamental chemotherapy (12.6 months) [5]. An orderly survey revealed improved average survival 33 vs. 12.5 months and 5-year survival 40% vs. 13% when contrasting CRS and HIPEC with palliative medical procedure and foundational chemotherapy [3].

**Cytoreductive Surgery and Hipec**

Intraabdominal hot chemotherapy is an emerging procedure for people with PM and includes meticulous aggressive surgery with hyper thermic intraperitoneal chemotherapy [6].

**Candidate for Hipec**

The HIPEC methodology is utilized to treat assortment cancers including colorectal, gastric, ovarian, mesothelioma, and appendiceal. It's anything but a bleeding edge treatment or a treatment of decision for somebody recently determined to have non-metastatic colon malignancy. In the event that you are thinking about HIPEC your age, general wellbeing, and above all, the stage and grade of your cancer are what aides your doctor determine if

this treatment option is right for you [4].

### **Cytoreductive Surgery**

Preceding getting HIPEC, your specialist will precisely evacuate all noticeable tumors inside your stomach depression. The person in question will likewise evacuate any organs with metastatic sicknesses, for example, the small digestive system, pancreas, ovaries. The specialist can likewise expel or burn little tumors from crucial organs (that can't be expelled), for example, you're liver, right now. Even if you have already had a bowel resection or debulking procedure for colon cancer in the past, you will need CRS to ensure maximum benefits from the HIPEC [3].

### **Hipec Procedures**

Immediately following the surgery while you are still asleep under anesthesia your surgeon performs the HIPEC procedure. Essentially, hyperthermic means "hot" not scalding, but hotter than your body temperature. The chemotherapy medications are warmed in light of the fact that it has been demonstrated that you can possibly expand the adequacy of the medications by warming them during conveyance.

The word intraperitoneal alludes to where the chemotherapy medications are directed. The inside of your abdomen is coated with a protective membrane called the peritoneum, which encompasses the peritoneal space, the zone where the majority of your stomach organs (bowels, liver and pancreas) are encased. The chemotherapy medications are siphoned into this space and permitted to essentially wash and drench it for as long as three hours. One common chemotherapy drug used for Hipec is Cisplatin, which sometimes is given with Mitomycin C, which is not a chemotherapy drug, but it is used to help slow the growth of certain cancers, such as colorectal cancer [5].

### **Controversial Issues**

The peritoneum is the third most successive site of colon cancer metastasis, and approximately 4%-7% of newly diagnosed patients with colon malignant growth are found to have peritoneal dissemination of the illness, despite the recent advances that facilitate early detection of the disease [6,7]. Peritoneal carcinomatosis from colorectal malignant growth origin has been related with poor anticipation as well as poor quality of life for the patients in this terminal phase of the disease [6,8]. Therefore, patients with colorectal malignant growth peritoneal carcinomatosis have been viewed as terminal, with only palliative surgery and or on the other hand fundamental chemotherapy being recommended [9].

Recently, in selected patients, the combination of broad cytoreductive surgery with Hyperthermic Intra-Operative Intraperitoneal Chemotherapy (HIPEC) has been accounted for to confer a benefit in survival of patients with peritoneal carcinomatosis from colorectal malignancy [10,11]. The first randomized trial comparing cytoreduction plus HIPEC pursued by foundational chemotherapy versus fundamental chemotherapy only, showed significant benefit from the combined treatment [3].

Among the factors that are related with prognosis in colorectal malignant growth patients with peritoneal metastasis undergoing CRS and HIPEC, despite the variations in chemotherapy regimens and techniques of hyperthermia [12]. The most significant ones that appear consistently in the literature are the fulfillment of cytoreduction and the degree of the disease, as measured using the peritoneal cancer growth file (PCI) [13-15].

Although the HIPEC regimen did not prove to be a significant independent prognostic factor in our patient sample, it comes in an era that the as of late displayed aftereffects of the PRODIGE 7 preliminary showed no benefit in overall survival for patients that received cytoreductive surgery combined with HIPEC using Oxaliplatin versus cytoreductive medical procedure alone. As one of the main criticisms of the study is the choice of the HIPEC regimen, it is evident that the comparison of survival outcomes between MMC and Oxaliplatin merits further investigation.

Last year a randomized phase III preliminary from France provides no survival benefits according to the findings. At a middle follow up of 63.8 months, middle by and large survival the essential endpoint of the examination was "completely comparable" at 41.7 and 41.2 months, separately, in 133 patients randomized to get HIPEC with oxaliplatin after cytoreductive medical procedure and 132 randomized to the cytoreductive medical procedure just arm, reported during the yearly gathering of the American Society of Clinical Oncology.

Middle generally backslide free survival was 13.1 and 11.1 months in the gatherings. The postoperative death rate was 1.5% at 30 days in the two gatherings, taking note of that no distinction was seen between the gatherings in the pace of symptoms during the initial 30 days after medical procedure. "However, we did find a difference between the two arms concerning late, severe complications within 60 days," stated, clarifying that the 60-day intricacy rate was nearly twofold in the HIPEC bunch versus the no-HIPEC gathering (24.1% vs. 13.6%).

Patients in the preliminary had organized IV colorectal cancer with secluded peritoneal carcinomatosis and a middle age of 60 years. They were selected and randomized at 17 focuses in France between February 2008 and January 2014. The survival pace of the medical procedure alone was out of the blue high and all colorectal disease patients with an isolated peritoneal carcinomatosis ought to along these lines be considered for medical procedure.

The crucial message from provide 7 trial is first the IMPORTANT role of cytoreductive surgery which in patients with PM offers a better survival when we compare with palliative surgery and systemic chemotherapy second the important role of Hipec in a low PCI<10 which offers a median survival of 60 months vs 44 months in CRS + systemic chemo and third the strong indication that mitomycin may offer better survival results versus oxaliplatin [16].

### **Conclusion**

Outcomes are more favorable from CRS and HIPEC when disease burden is lower. A pro-active approach to identify early CRPM with a "second look This article is protected by copyright. All rights reserved. Page 4 of 6 laparotomy" with CRS and HIPEC six months after high-risk resections led to detection of CRPM in 55% of patients, all of whom were asymptomatic [17]. Other novel approaches include the use of prophylactic or adjuvant HIPEC in high-risk cancers. However, more high-level evidence is required before these novel approaches can be brought into standard treatment. The results of randomized clinical trials such as ProphylChip (NTC01226394) and COLOPEC (NCT02231086) will help better define the role of such pro-active approaches. It is reassuring that colorectal surgeons, regardless of seniority, have a similar approach to managing CRPM. CRS and HIPEC is the standard of care for CRPM in many countries. In Australia, the Cancer Council guidelines recommend referral to a peritonectomy center for consideration of CRS and HIPEC for CRPM [18].

CRS and HIPEC have proven benefit and offer a proportion of patients with a realistic glimmer of hope. Unfortunately, the majority of patients have high disease burden, and are not candidates for CRS and HIPEC. There is an urgent need to seek new therapies to help improve survival in the unresectable. In recent years, with advances in pre-clinical modeling of disease and immunotherapies, novel approaches such as personalized medicine or palliative options such as Pressurized Intra-Peritoneal Chemotherapy (PIPAC) may be options to explore in the future [19,20].

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