MedCrave
Step into the World of Research

Journal of Cancer Prevention & Current Research

Management of Peritoneal Metastases of Colorectal Cancer, Literature Review

Abstract

Background: Management of peritoneal metastases from colorectal cancer is a highly debatable subject. Treatment options of this disease range from systemic chemotherapy, surgery followed by chemotherapy to resection, then chemotherapy and intraperitoneal chemotherapy with hyperthermia.

Aim of the study: To review guidelines and updated studies on management of peritoneal carcinomatosis caused by colorectal cancer.

Methodology: The study includes review of systematic reviews, multi-institutional data collection, randomized controlled trials and clinical reviews.

Results: A total number of 893 patients with advanced colon cancer who presented as stage IV with peritoneal metastases as first presentation have been involved in this study. The most significant finding in these studies is the role of systemic chemotherapy either given as neoadjuvant, adjuvant or combined modality. The addition of Bevazucimab as vascular endothelial growth factor (VEGF) was a significant factor in improving response rate and survival. The use of Mitomycin C (MMC) as a component of HIPEC: hyperthermic intraperitoneal chemotherapy) was better than Oxaliplatinin terms of median overall survival.

Conclusion: The best treatment strategy for these patients is to give neoadjuvant chemotherapy (no specific regime showed superiority over others) with VEGF Bevazucimab aiming at maximum cytoreduction, and then doing HIPEC using Mitomycin C as chemotherapeutic agent followed by adjuvant chemotherapy including Bevazicumab as VEGF component.

Keywords: Colorectal cancer; Peritoneal metastases; Chemotherapy; Surgery; Hyperthermia

Review Article

Volume 2 Issue 6 - 2015

Ehab Esmat Fawzy*

Department of clinical oncology, Cairo University, Saudi Arabia

***Corresponding author:** Ehab Esmat Fawzy, Professor of clinical oncology faculty of Medicine, Cairo University, Saudi Arabia, Tel: 4169039323; Email: ehabesmatf@yahoo.com

Received: May 08, 2015 | **Published:** June 04, 2015

Abbreviations: VEGF: Vascular Endothelial Growth Factor; MMC: Mitomycin C; HIPEC: Hyperthermic Intraperitoneal Chemotherapy

Introduction

10% -15% of patients initially diagnosed with colorectal cancer have peritoneal deposits at time of initial diagnosis [1]. Peritoneum represents the next place of metastatic disease in colorectal cancer after liver [2]. For long time, peritoneal metastases of colon cancer is considered a terminal stage disease with palliative care as the only modality for this disease [3]. In addition to the poor overall survival of patients with colon cancer who present with peritoneal metastases, there are no definite treatment strategies for this group of patients [4].

Purpose of the Study and Rationale

The main purpose of this study is to find the best treatment strategy of colon cancer with peritoneal carcinomatosis. I reviewed the current state of art policies and treatment guidelines for colorectal peritoneal carcinomatosis, aiming to reach a reasonable treatment approach helping these patients to achieve better response and survival.

Methodology

An internet web search for all high quality and evidence based sites like Pubmed, Medline, and Ovid. Search words included: Cancer Colon peritoneal carcinomatosis, surgery, chemotherapy, hyperthermia, 2014, prospective. High rank research publications including but not limited to; systematic reviews, meta-analysis, prospective randomized studies, cohort studies, and case reports. A proper organization of articles based on its relevance to the subject, date of publications, power of the study, and rank of journal.

Results

Cochrane review, 5 articles, non-related, Pubmed search 1164 articles search words : colorectal peritoneal carcinomatosis, 660 articles with the search :colorectal peritoneal carcinomatosis chemotherapy, 551 articles with the search colorectal peritoneal carcinomatosis chemotherapy surgery, 241 articles with the search colorectal peritoneal carcinomatosis chemotherapy hyperthermia, 31 articles with the search colorectal peritoneal carcinomatosis chemotherapy surgery hyperthermia 2014. 14 articles with colorectal peritoneal carcinomatosis chemotherapy surgery hyperthermia 2014 prospective.

A total number of 893 patients with advanced colon cancer who presented as stage IV with peritoneal metastases as first presentation have been involved in this study. After review of current literature dated till 2014 and using Ovid, Medline and Pubmed search engines, only 4 research articles have been chosen [5-8]. Two articles were prospective non randomized cohort studies Ceelen W et al. [6] and Passot G et al. [7], one retrospective study Villaverde et al. [5] and one review study Kuijpers A et al. [8].

The most significant finding in these studies is the role of systemic chemotherapy either given as neoadjuvant, adjuvant or combined modality, as seen by Passot G et al. [7] and Kuijpers A at al. [8], in both studies, patients who received neoadjuvant systemic chemotherapy achieved the highest 5 years overall survival rates (75%) [7] which is incredibly high as compared to known figures of 11 % [9].

Furthermore, the choice of systemic chemotherapy regimen was a significant factor in disease response / survival as shown by Ceelen W et al. [6] whereby the median overall survival (MOS) was significantly higher in neoadjuvant chemotherapy and Bevacisumab versus those under chemotherapy alone (P =0.021). Disease burden was also a strong independent prognostic variable with the highest response and survival rates among those who presented with minimal or low disease burden. So Passot G et al. [7] found that Pcr (Pathological complete response) induced by neoadjuvant chemotherapy is an independent prognostic factor for 5 years overall survival rates (75%). No other factors affect MOS. The only contribution of HIPEC in response rate/ survival was in the type of chemotherapy chosen for HIPEC, so Villaverde et al. [5] found that, MOS: 54.3 was months in MMC (mitomycin group) , and 28.2 months in Oxaliplatin group (both groups has low volume peritoneal disease) (Table 1).

Table 1: Summarizes the findings in reviewed articles related to the subject of research.

Study Author	Methodology	Number of Patients	Treatment Arm (s)	Results
Villaverde et al. [5]	Retrospective study	539	a. HIPEC (a) with MMC (b) b. HIPEC with Oxaliplatin	MOS: 54.3 months in MMC group, and 28.2 months in Oxaliplatin group (both groups has low volume peritoneal disease).
Ceelen W et al. [6]	Prospective Non-Randomised	166	a. HIPEC with neoadjuvant chemotherapy alone. b. HIPEC with neoadjucant chemotherapy and Bevazicumab	MOS was significantly higher in neoadjuvant chemotherapy and Bevacisumab versus those under chemotherapy alone (P: =0.021).
Passot G et al. [7]	Prospective Non-Randomised	115	a. Neoadjuvant Irinotecan then surgery +/- HIPEC b. Neoadjuvant Oxaliplatin then surgery +/- HIPEC	Pcr (d) induced by neoadjuvant chemotherapy is an independent prognostic factor for 5 years over all survival rates (75%). No other factors affect MOS
Kuijpers A et al. [8]	Review article	73	a. Neoadjuvant chemotherapy + CRS (e) + HIPEC+ adjuvant chemotherapy. b. Neoadjuvant chemotherapy + CRS(e)+ HIPEC c. CRS(e)+ HIPEC+ adjuvant chemotherapy d. Only CRS(e)+ HIPEC	The least PFS (f) and MOS were found in group 4 (who did not get any systemic chemotherapy. (PFS: 15 versus 4 months, *P* = 0.024; OS: median 30 versus 14 months, *P* = 0.015)

HIPEC: Cytoreductive Surgery and Hyper Thermic Intra Peritoneal Chemotherapy; MMC: Mitomycin C Chemotherapy; MOC: Median Overall Survival; PCR: Pathological Complete Response; CRS: Cytoreductive Surgery; PFS: Progression Free Survival

Discussion

Patients diagnosed with colon cancer are staged as stage IV (M1B) if they have peritoneal metastases. A poor survival rate (11%) 5 years overall survival has been found for this stage of colon cancer [9]. Even a more conservative figures of poor survival rates for this stage of colon cancer have been published (5 years survival rates of 0 % and median survival rate of 6-8 months) [10,11]. One of the major prognostic factors of survival in patients with colon cancer and peritoneal metastases is extent of disease, which is shown clearly in many research articles [12]. So it's prudent to treat those patients with maximal cytoreduction in addition to other treatment options like neoadjuvant, and adjuvant chemotherapy and HIPEC [13].

From review of current literature it seemed that the best treatment options for these patients is to attempts systemic treatment (either preoperative, postoperative chemotherapy , or both) as seen by Passot G [7], and Kuijpers A et al. [8], in both studies, patients who received neoadjuvant systemic chemotherapy achieved the highest 5 years overall survival rates (75%) Passot G et al. [7], which is incredibly high as compared to known figures of 11 % [9]. On the other hand, Kuijpers A et al. [8] found that; the least PFS and MOS was found in a group of patients who did not get any systemic chemotherapy as compared to those who received systemic chemotherapy (PFS: 15 versus 4 months, *P* = 0.024; OS: median 30 versus 14 months, *P* = 0.015) for those who received systemic chemotherapy (either neoadjuvant, adjuvant chemotherapy or both respectively.

The choice of systemic chemotherapy either in neoadjuvant, adjuvant setting or both can affect disease response and survival, so Ceelen W et al. [6] found that the addition of vascular endothelial growth factor (VEGF) Bevazicumab adds an advantage to the MOS, which was shown as a significantly higher MOS in neoadjuvant chemotherapy and Bevacisumab versus those under chemotherapy alone (P: =0.021). Not only the choice of systemic chemotherapy had an influence on response and survival of these patients, but also the choice of chemotherapeutic agent for HIPEC, as shown by Villaverde et al. [5], who found that, the MOS was 54.3 months in MMC group, and 28.2 months in Oxaliplatin group (both groups has low volume peritoneal disease).

Conclusion

The best treatment option for patients with cancer colon and

peritoneal metastases has to be more researched to achieve the best response rate and survival. From current review of literature (as of 2014 research data), the best treatment strategy for these patients is to give neoadjuvant chemotherapy (no specific regime showed superiority over others) with VEGF Bevazucimab aiming at maximum cytoreduction, then doing HIPEC using Mitomycin C as chemotherapeutic agent followed by adjuvant chemotherapy including Bevazicumab as VEGF component.

Recommendation

It's recommended to do more prospective studies on these patients with advanced colon cancer and peritoneal metastases adding different chemotherapeutic agents (lie Capecitabine), targeted agents (like Ceutximab) and may be changing the technique or chemotherapeutic agents in HIPEC.

References

1. Dawson LE, Russell AH, Tong D, Wisbeck WM (1983) Adenocarcinoma of the sigmoid colon: Sites of initial dissemination and clinical patterns of recurrence following surgery alone. J Surg Oncol 22(2): 95-99.
2. Knorr C, Reingruber B, Meyer T, Hohenberger W, Stremmel C (2004) Peritoneal carcinomatosis of colorectal cancer: Incidence, prognosis, and treatment modalities. Int J Colorectal Dis 19(3): 181-187.
3. Chu DZ, Lang NP, Thompson C, Osteen PK, Westbrook KC (1987) Peritoneal carcinomatosis in non gynecologic malignancy: A prospective study of prognostic factors. Cancer 63(2): 364-367.
4. Sadeghi B, Arvieux C, Glehen O, Beaujard AC, Rivoire M, et al. (2000) Peritoneal carcinomatosis from non-gynecologic malignancies: Results of the EVOCAPE 1 multicentric prospective study. Cancer 88(2): 358-363.
5. Prada-Villaverde A, Esquivel J, Lowy AM, Markman M, Chua T, et al. (2014) The American Society of Peritoneal Surface Malignancies evaluation of HIPEC with Mitomycin C versus Oxaliplatin in 539 patients with colon cancer undergoing a complete cytoreductive surgery. J Surg Oncol 110(7): 779-785.
6. Ceelen W, Van Nieuwenhove Y, Putte DV, Pattyn P (2014) Neoadjuvant chemotherapy with bevacizumab may improve outcome after cytoreduction and hyperthermic intraperitoneal chemo perfusion (HIPEC) for colorectal carcinomatosis. Ann Surg Oncol 21(9): 3022-3028.
7. Passot G, You B, Boschetti G, Fontaine J, Isaac S, et al. (2014) Pathological response to neoadjuvant chemotherapy: a new prognosis tool for the curative management of peritoneal colorectal carcinomatosis: Ann Surg Oncol 21(8): 2608-2614.
8. Kuijpers AM, Mehta AM, Boot H, van Leerdam ME, Hauptmann M, et al. (2014) Perioperative systemic chemotherapy in peritoneal carcinomatosis of lymph node positive colorectal cancer treated with cytoreductive surgery and hyperthermicintraperitoneal chemotherapy. Annals of Oncology 25(4): 864-869.
9. American Cancer Society (2015) what are survival rates of colorectal cancer by stage? Colorectal Cancer.
10. Sadeghi B, Arvieux C, Glehen O, Beaujard AC, Rivoire M, et al. (2000) Peritoneal carcinomatosis from non-gynecologic malignancies: Results of the EVOCAPE 1 multicentric prospective study. Cancer 88(2): 358-363.
11. Jayne DG, Fook S, Loi C, Seow-Choen F (2002) Peritoneal carcinomatosis from colorectal cancer. Br J Surg 89(12): 1545-1550.
12. Glehen O, Kwiatkowski F, Sugarbaker PH, Elias D, Levine EA, et al. (2004) Cytoreductive Surgery Combined With Perioperative Intraperitoneal Chemotherapy for the Management of Peritoneal Carcinomatosis From Colorectal Cancer: A Multi-Institutional Study. J Clin Oncol 22(16): 3284-3292.
13. Sugarbaker PH (1995) Peritonectomy procedures. Ann Surg 221(1): 29-42.

Citation: Fawzy EE (2015) Management of Peritoneal Metastases of Colorectal Cancer, Literature Review. J Cancer Prev Curr Res 2(6): 00057. DOI: 10.15406/jcpcr.2015.02.00057