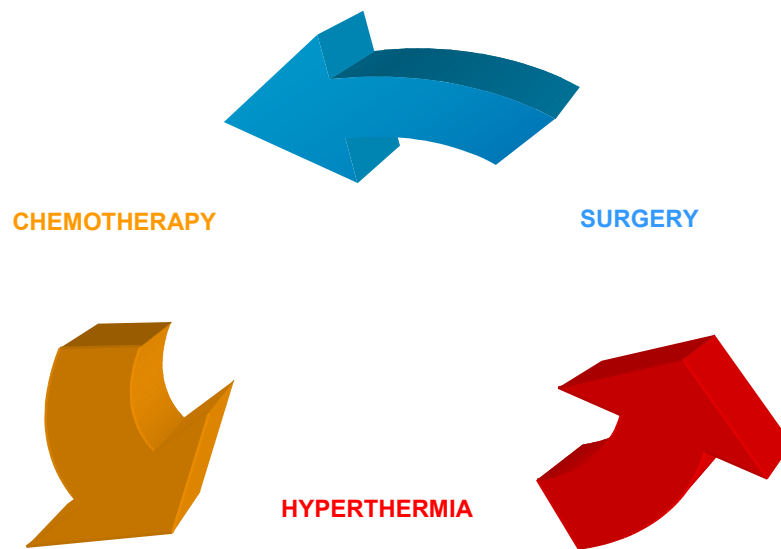


HIPEC AND OVARIAN CANCER

Ovarian cancer originates from the surface lining of the ovaries and also from the peritoneum, the lining of the ‘bag’ which surrounds the contents of the abdomen and pelvis. Growth of ovarian cancer is most often relatively silent and by the time of diagnosis it has usually spread throughout the peritoneal cavity. Standard treatment for ovarian cancer is surgery followed by chemotherapy with a combination of two types of chemotherapy agent, platinum and a taxane. Although response rates of ovarian cancer to this initial chemotherapy are high, 60-70% of all patients with ovarian carcinoma will recur, with the overall 5-year survival still being only around 50%.



HIPEC (hyperthermic intraperitoneal chemotherapy) incorporates three modalities of treatment as shown in the diagram above: surgery and intraperitoneal chemotherapy which have proven roles in the treatment of ovarian cancer and heat which has theoretical advantages. The surgical excision of tumors to reduce the bulk of residual disease prior to chemotherapy is the standard initial treatment for ovarian cancer and has a role in some patients with recurrent disease. Intraperitoneal delivery of chemotherapy involves inserting the chemotherapy agents directly within the peritoneal ‘bag’. This means the chemotherapy agents have the potential to directly reach all areas of the peritoneal cavity where the ovarian cancer remains ‘contained’ for long periods. Intraperitoneal delivery of chemotherapy at normal temperatures in ovarian cancer has been shown to be effective in front-line treatment. Three large, randomized studies investigating the intraperitoneal delivery of cisplatin, carboplatin or

paclitaxel in combination with intravenous delivery have shown a survival advantage for patients treated with intraperitoneal chemotherapy. Hyperthermia, on its own, is tumoricidal. In addition, it increases the ability of some chemotherapy agents to kill cancer cells and allows these agents to penetrate more deeply into tumor implants.

Ovarian carcinoma is a logical target for directed intraperitoneal therapy in combination with heat and there are reports of clinical studies looking at HIPEC following surgical debulking in this disease. HIPEC could have a role to play at several of the natural history 'time-points' of ovarian cancer including at the time of initial surgery, for consolidation following initial therapy and for recurrent disease.

If HIPEC were to be performed at the time of initial surgery the advantages would be that intraperitoneal adhesions would have all been divided allowing chemotherapy to reach all areas of the peritoneal cavity and any residual tumor would be at the smallest possible volume. The tumor would also be exposed to chemotherapy many days prior to the usual time following recovery from surgery. HIPEC might play a role in reducing the chance of recurrence following front-line treatment. The most recent large randomized study comparing standard intravenous chemotherapy with combined intravenous/intraperitoneal chemotherapy at normal temperatures showed a significantly improved median survival from 49 to 65 months in those patients receiving part of their chemotherapy through the intraperitoneal route. However, 65% of patients in this arm experienced recurrence of their disease within the duration of the study. It is possible that HIPEC given following front-line therapy when there is no detectable disease for what is called 'consolidation' might have a role. Recurrent ovarian cancer has a relatively poor prognosis but there is evidence that some highly-selected patients benefit from extensive surgery to remove all disease. In these patients HIPEC would have theoretical advantages given at the time of surgery.

HIPEC is an exciting development which needs to be continued to be researched to evaluate its role in improving outcomes in ovarian cancer.

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