# Surgical Treatment of Metastatic Colorectal Cancer

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#### **KEYWORDS**

• Stage IV • Colorectal cancer • Metastases • Surgical management • Surgery

#### **KEY POINTS**

- Surgical treatment of metastatic colorectal cancer offers a chance for cure or prolonged survival.
- Advanced surgical techniques, adjuncts to resection, and modern chemotherapy all
  contribute to best outcomes for patients with hepatic metastases.
- Patients with peritoneal metastatic disease may benefit from surgical cytoreduction and intraperitoneal chemotherapy (HIPEC). Best outcomes are achieved in those for whom complete cytoreduction is surgically feasible.
- Pulmonary metastases are rarely isolated yet surgical resection is associated with prolonged survival in selected patients.

#### MANAGEMENT OF METASTATIC COLORECTAL CANCER

Metastatic disease occurs in half of people with colorectal cancer (CRC). Metastasis spread through hematogenous or lymphangitic routes and may occur in lymph nodes, liver, lung, peritoneum, brain, and bone. Synchronous presentation at the time of diagnosis of the primary tumor occurs in 21% of patients and is associated with worse survival compared with those who present with metachronous disease. For patients who present with advanced-stage disease and receive no treatment, the median life expectancy is 9 months and 5-year survival is 3%. Improvements in therapy over the past 15 to 20 years have led to improved outcomes because even those who can receive chemotherapy only

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#### Abbreviations

CALI Chemotherapy-associated liver injury

CC Completeness of cytoreduction

CEA Carcinoembryonic antigen

CRC Colorectal cancer

CRLM Colorectal liver metastasis
CRS Cytoreductive surgery
CT Computed tomography

DFS Disease-free survival

EGFR Epidermal growth factor receptor

FUDR 5-fluoro 2-deoxyuridine

HIPEC Hyperthermic intraperitoneal chemotherapy

HR Hazard ratio

MWA Microwave ablation
OS Overall survival

PC Peritoneal carcinomatosis
PCI Peritoneal carcinomatosis index

RFA Radiofrequency ablation

have a median survival of 30 months.<sup>3</sup> Furthermore, multimodal therapies in some cases may even provide cure in the setting of metastatic disease. Understanding the natural history of metastatic CRC in the context of patient- and tumor-specific factors is critical to making treatment decisions when there are a variety of options.

Although most patients with metastatic CRC are incurable, the combination of modern chemotherapy with improved surgical and radiation therapy techniques has led to prolonged cancer control and extended survival for many. Staging work-up for metastatic disease includes computed tomography (CT) of the chest, abdomen, and pelvis with consideration of PET/CT for selected patients with indeterminate findings. Routine laboratory work-up, carcinoembryonic antigen (CEA) level, and determination of RAS and BRAF status of the primary tumor should be performed. Biopsy of metastasis may be needed, or preferred, in the setting of first recurrence or again with indeterminate imaging findings. A multidisciplinary evaluation is of critical importance for most patients with metastatic CRC because choice and order of therapies differ depending on presentation, number of sites and location of metastases, and potential for surgical resection.

#### Genetic Mutation and Sites of Metastasis

Stage IV CRC encompasses a wide range of possibilities with strikingly different patterns of disease presentation and progression. Prognosis declines as number of metastatic sites of increases and staging has been changed to reflect this heterogeneity. The American Joint Committee on Cancer seventh edition in 2010 changed stage IV disease to subcategories of IVA (metastasis to one site) and IVB (metastasis to more than one site). Although this distinction denotes a difference in overall survival (OS), there is yet more diversity because site of metastasis and the possibility of surgical resection also help determine prognosis. The chance of developing metastasis increases with worse primary tumor T and N stage. In general, potentially curative treatments are the goal for patients with one site of surgically resectable metastatic disease especially in the metachronous setting. For those with more than one site of metastatic disease, the general goal is cancer control.

Underlying molecular mechanisms explaining the exact route of metastatic spread of CRC have not yet been determined. There is a high concordance of genetic mutations between primary and metastatic tumors, and sequencing of the primary tumor for RAS, BRAF, and PIK3CA has actionable consequences for metastatic disease in

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