

## LIVER METASTASES IN COLORECTAL CANCER

### Epidemiology

- Colorectal cancer is the third leading cause of cancer death in the US
- 53.7 cases colorectal cancer per 100,000 population per year
- ~20% have synchronous liver metastases
- ~20% more will develop metachronous lesions within next 3 years
- Untreated these patients have very poor prognosis (3 year survival 3%; virtually no 5 yr survival)
- Only 10-20% resectable

### Diagnosis

- pretreatment imaging to determine tumor size, location, relationships to major intrahepatic vascular structures, presence of extrahepatic disease, and estimation of postresection residual liver parenchyma volume
- MRI and CT scan
  - Equivalent sensitivity for lesions greater than 2 cm, but MRI significantly better for imaging lesions < 2cm
- PET scan
  - May detect lesions missed on MRI or CT
- Intra-operative Ultrasound
  - May also detect lesions not seen on MRI

### Contraindications to Resection

- Absolute:
  - extrahepatic disease (exception is anastomotic site recurrence in colon and limited pulmonary metastases – these can be resected concomitantly)
  - impossibility of removing entire tumor while leaving sufficient functional liver parenchyma (at least 30%); partial resection provides no benefit
- Relative:
  - Lymph node involvement, synchronous presentation, multiple tumors, bilobar involvement, CEA elevation > 200 ng/ml, involved histologic margins

### Hepatic Resection

- Operative mortality 2-5%
- 5 year survival 25 – 37% (37% in largest trial – 1001 patients)
- 10 year survival 20 – 26%
- Survival based on pre-op risk factors: Positive margin, Extra-hepatic disease, Node positive primary, Disease free interval < 1yr, Number of hepatic tumors > 1, Largest hepatic tumor > 5cm, CEA > 200 ng/ml

**Clinical Risk Score and Survival in 1001 Patients Undergoing Liver Resection for Metastatic Colorectal Cancer<sup>2</sup>**

Score	1-Yr Survival (%)	3-Yr Survival (%)	5-Yr Survival (%)	Median Survival (mo)
0	93	72	60	74
1	91	66	44	51
2	89	60	40	47
3	86	42	20	33
4	70	38	25	20
5	71	27	14	22

\* Each of the following five risk factors equals one point: node-positive primary, disease-free interval less than 12 months, more than 1 tumor, size greater than 5 cm, carcinoembryonic antigen level greater than 200 ng/mL. Score is total number of points in an individual patient.

Methods to Improve Resectability

- Neoadjuvant chemotherapy – may shrink the tumor to a respectable size
  - provides hope of long-term survival similar to primarily resected patients
- Portal Vein Embolization
  - induces a compensatory hypertrophy of the future remnant liver, enabling more confident resection of tumors with clear margins
  - resection usually 4-6 weeks after embolization
- Local destructive therapy
  - Cryotherapy/radiofrequency ablation (RFA) – can be used to get multiple, smaller mets while resecting a larger metastasis
- 2-stage or repeat hepatectomies

Chemotherapy

- Sole therapy
  - Irinotecan, 5-FU, leucovorin, bevacizumab – 2 year survival 40%
- Neoadjuvant – may shrink tumor to a resectable size
- Adjuvant: Hepatic artery pump (FUDR) + systemic vs. systemic alone
  - Significantly lower recurrence rate and survival advantage at 2 years with infusion pump
  - Complication of pump – infection, hepatic artery thrombosis, dislodged catheter, perfusing outside liver or only part of liver, biliary obstruction

Radiofrequency Ablation (RFA)

- Percutaneous, intra-op, or laparoscopic
- feasible for tumors less than 3 cm in diameter
- can be used to treat mets close to major intrahepatic vessels but not bile ducts
- local recurrence 9-39%
- New metastases 27-66%

- Median survival 36 months

### Conclusions

- Resect whenever possible
  - Worst resection cases do better than best chemo
- Unresectable cases
  - Neo-adjuvant therapy to attempt to make it resectable; then resect if successful
  - RFA if unresectable unable to adequately shrink

### References

1. Adam R, Lucidi V, Bismuth H: Hepatic colorectal metastases: methods of improving resectability. Surg Clin North Am 84, 2004
2. Khatri VP, McGahan J: Non-resection approaches for colorectal liver metastases. Surg Clin North Am 84, 2004
3. Fong Y, Fortner J, Sun RL, et al: Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: Analysis of 1001 consecutive cases. Ann Surg 230:309-321, 1999.
4. Kemeny N, Huang Y, Cohen AM, et al: Hepatic arterial infusion of chemotherapy after resection of hepatic metastases from colorectal cancer. N Engl J Med 341:2039-2048, 1999.
5. D'Angelica M, Fong Y: The Liver. In Townsend CM, editor: Sabiston Textbook of Surgery, 17<sup>th</sup> ed, Philadelphia 2004, Elsevier Saunders

Marcus Malek, MD  
March 21, 2005