

PULMONARY METASTASES IN COLORECTAL CANCER

Staging and Prognosis

- There are several classification systems including Dukes' but the Tumor Node Metastases (TNM) system is the most widely accepted system in the US

TNM System	Modified Dukes' System	5 Year Survival (%)
Stage 0: T _{IS} , N ₀ , M ₀ Stage 1: T ₁ /T ₂ , N ₀ , M ₀	Stage A	>90
Stage 2: T ₃ /T ₄ , N ₀ , M ₀	Stage B	60-80
Stage 3: Any T, N ₁ /N ₂ , M ₀	Stage C	20-50
Stage 4: Any T, Any N, M ₁	Stage D	<5

Epidemiology

- Colorectal cancer is the second most common malignancy in western countries. The lifetime chance of a newborn infant in the US today developing CRC is 5%.
- The most common types of metastases in colorectal cancer are to the liver and lungs and hepatic and pulmonary metastases are frequently associated.
- About 10-25% of patients with colorectal CA develop pulmonary metastases but only 2-4% have metastasis confined just to the lungs

Clinical Presentation

- Most patients are asymptomatic. Symptoms are only reported in 10-20% of cases and reflect proximity to central airways. They include:
 - cough and hemoptysis, the most frequent complaints.
 - also pneumonia, pleuritic chest pain and dyspnea can be observed.

Diagnosis

- Imaging
 - CXR is usually the first modality in diagnosis.
 - Helical CT is the best modality (good sensitivity, poor specificity). Lung biopsy is usually not necessary after CT scan. CT can also demonstrate pulmonary metastases in 5-10% of patients with a normal CXR.
 - Mets typically appear as smooth, well circumscribed and peripherally located nodules. On CT they are hypodense and rounded. Calcified lesions are more inflammatory in etiology.
 - Bronchoscopy, mediastinoscopy and sputum cytology can all be useful to assess the histologic nature of the pulmonary metastases
- Labs
 - **CEA:** CEA is a glycoprotein absent from normal adult intestinal mucosa but present on primitive endoderm. It is not useful as a screening tool.
 - It is more useful in assessing prognosis of people already carrying the diagnosis. Assessing pre-op and post-op CEA levels might help identify patients who might benefit from early adjuvant therapy.

Treatment

• Surgical Resection

- Surgical resection is considered definitive therapy. However, only 2-4% of pulmonary metastases can be treated surgically and only about 1% of hepatic metastases.
- Factors affecting survival following resection are:
 - Number of lesions
 - Stage of primary tumor
 - Disease free interval (DFI)
 - High prethoracotomy CEA
 - Involved thoracic or mediastinal lymph nodes.
- There is no difference between the site of the primary (rectum or colon) and the prognosis after resection - though rectal more frequently gives rise to pulmonary metastases because of its dual drainage (caval and portal).
- Surgical resection of a single metastasis is widely accepted particularly when the tumor can be resected completely. Pulmonary resection for bilateral or multiple metastases is still controversial.
- Age, sex and gender do not affect prognosis.
- Patients with single metastases, (DFI) >36 months and normal preoperative CEA have good statistically significant prognostic indicators. Thoracic or mediastinal lymph node involvement is a poor prognostic sign.
- Indications: Appears very case based
 - Younger patients as they tolerate surgery better though some studies show negative data
 - Number of metastases up to 3 can be resected and treated as one single spreading.
 - Well differentiated tumors. Poorly differentiated tumors may have more diffuse spread.
 - A margin of resection between tumor and clean parenchyma of at least one cm though standards vary
 - Dukes' Class A/B have a better prognosis compared to Dukes' class C tumors.
 - Longer intervals between the colon resection and metastatectomy i.e. the disease free interval (DFI) >10months is associated with a better prognosis.
 - CEA < 5ng/ml
- Contraindications
 - metastases greater than 3 in number i.e. extensive pulmonary disease though not an absolute contraindication.
 - both extra-hepatic and extra-pulmonary mets
 - lymph node metastases of the hepatoduodenal ligament

• Chemotherapy

- Chemotherapy in colorectal cancer metastases is controversial.
- Active agents used include 5-FU, irinotecan and oxaliplatin

- The role of adjuvant chemotherapy is unclear and there is currently no data supporting the use of the newer agents such as oxaliplatin and irinotecan for adjuvant chemotherapy.
- Duration of treatment is controversial ranging from 12-24 weeks. Most physicians go 1-2 cycles beyond the best response.
- There might be a role for neoadjuvant treatment in advanced but not disseminated disease (stage II-III) when the primary has been completely resected.

Outcome

- Patients with untreated metastatic colorectal cancer have a median survival of less than 10 months with a 5 year probability of survival of less than 5%.
- In patients with just lung metastases, surgery provides long-term 5 year survival rates from 20-40% of patients with an operative mortality of 1% or less and repeat lung resections for recurrent disease show similar rates.
- 5 year survival is 43.6% for patients with one metastatectomy and 34% for patients with multiple ones
- 5 year survival for patients with DFI > 36months =55%,DFI >12-35 months = 38.6% and DFI > 10-11 months =22.6%
- 5 year survival for patients with normal pre-op CEA =58.2% and 0% for pts with CEA >5ng/ml pre-op
- One study from the Mayo clinic reported 5 year survival rates of 36.9% for solitary nodules, 19.3% for 2 nodules and 7.76% for more than 2 nodules.

Pulmonary Metastases from other GI Sources

- Pulmonary metastases also arise from the stomach and pancreas. CXR is used for diagnosis and therapeutic monitoring though CT is the most sensitive and detects a higher number of nodules compared to other modalities.
- The literature is unclear but surgical resection appears case based with a limited therapeutic advantage. However, it cannot be totally excluded since it is often necessary to differentiate between primary and secondary pulmonary nodules.

References

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August 2005