

Management of the primary in Stage IV colorectal cancer



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Stage IV Colorectal Cancer

- 15%-20% CRC patients present with Stage IV disease
- Treatment decision making challenging
 - Liver mets
 - Colon/Rectal Primary
 - Optimal timing and sequence of interventions
- Treatment strategy influenced by:
 - potential resectability of the liver
 - symptom pattern of the primary

Assessment of the liver: Resectable, borderline or unresectable

- Accurate assessment of the liver is essential:
 - intent of treatment (curative vs palliative)
 - timing and sequence of treatment
- Many modalities to treat liver metastases
 - Surgery +/- PVE
 - Chemotherapy
 - Radiofrequency ablation (RFA)
 - Intra-arterial chemotherapy

Assessment of the liver: Resectable, borderline or unresectable

- Synchronous mets, multiple mets and bilobar disease no longer contraindications to resection
- Assessment of liver mets by HPB surgeon necessary
 - Resectable - Curative
 - Borderline - Possibly curative
 - Unresectable - Palliative

Current Approaches to the Liver

- Traditional - primary followed by liver
- Simultaneous - primary and liver together
 - 5 year survival ~30-40%
- “Liver first approach”
 1. Pre-operative chemotherapy
 2. Liver
 3. Primary
 - Patient outcome related to progression of liver mets
 - Avoids delay in treatment of liver metastasis from:
 - Complications from colorectal surgery
 - Long course chemoradiation for rectal cancer
 - Minimal data available

Assessment of the Primary Symptomatic or Asymptomatic?

- Symptomatic
 - Perforation
 - Bleeding - transfusion dependent
 - Obstruction requiring admission or “impending obstruction”
 - Scope does not pass through tumour
 - Proximal bowel dilatation on imaging
- Asymptomatic
 - Most not truly asymptomatic
- Bottom line is that it is often a judgement call

Definitely resectable

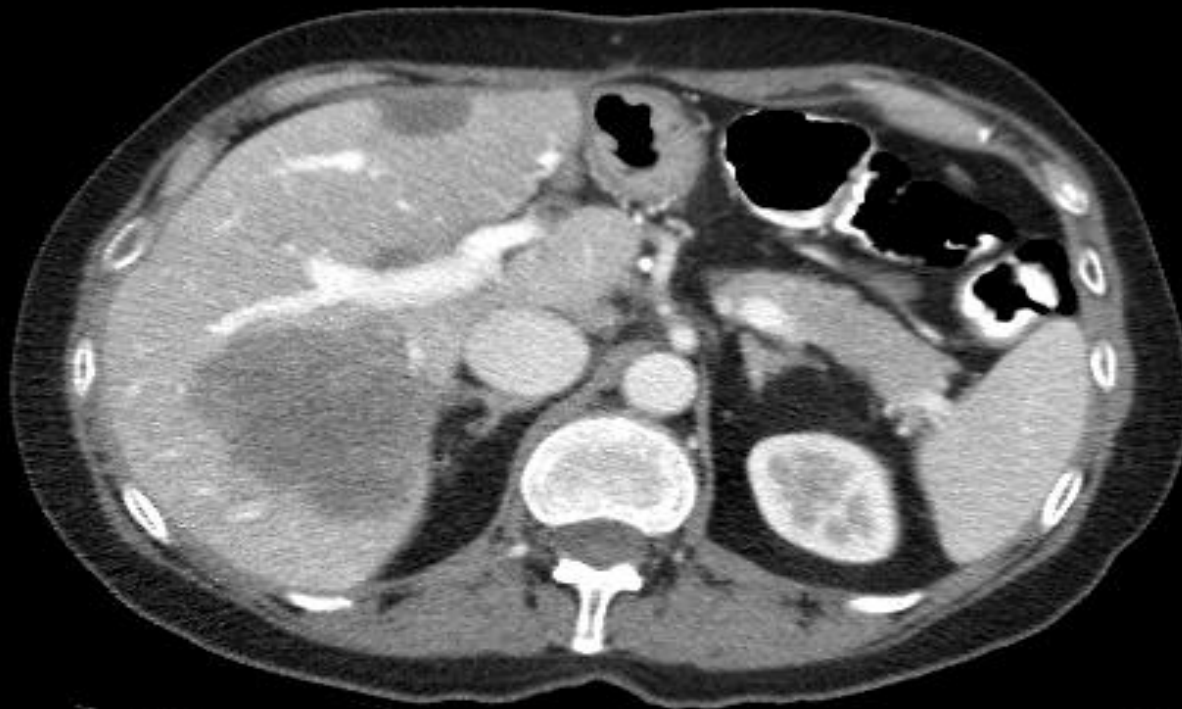
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Liver - Definitely Resectable – Curative Intent

Symptomatic	Asymptomatic
Traditional approach	Traditional approach (Liver first approach)
CONSIDERATIONS: <ul style="list-style-type: none">•Low threshold for protective stoma (avoid complications)•Simultaneous resection in select cases•Short course radiation for rectal cancer	

Borderline (potentially resectable)



Liver – Borderline - Potentially curable

Symptomatic	Asymptomatic
<p>Need chemotherapy ASAP</p> <p>Surgery to:</p> <ul style="list-style-type: none">•minimize complications•promote fast recovery <p><i>Colon</i></p> <p>R side - resect</p> <p>L side – resect + divert</p> <p><i>Rectum</i></p> <p>Diversion only</p>	<p>Liver first approach (Traditional approach)</p>

“Liver First Approach” for patients with locally advanced Stage IV rectal cancer

Verhoef, Diseases of the Colon and Rectum 2009;52:23-30

- 23 consecutive patients, 2003-2007
- Synchronous liver mets – locally advanced rectal cancer (T3-T4)
- Single centre, prospective study
 1. Neoadjuvant chemotherapy
 - 5FU + (oxaliplatin or irinotecan) +/- avastin X 2-3 cycles
 2. Liver resection (3 weeks after chemo; 6 weeks if avastin)
 3. Chemoradiation for primary tumour
 4. TME

<i>Median age, yrs</i>	58 (43-78)
Sex	
Male	15
Female	8
<i>Presentation</i>	
Obstruction	6
Pain	1
Blood loss/bowel habit	16
<i>Number of mets</i>	
≤ 3	14
>3	9
<i>Size of mets</i>	
< 5 cm	20
≥ 5 cm	3
<i>Bilobar disease</i>	
Yes	12
No	11
<i>CEA</i>	
< 5	5
≥ 5	18

“Liver First Approach” for patients with locally advanced Stage IV rectal cancer

Verhoef, Diseases of the Colon and Rectum 2009;52:23-30

- 15 patients – partial response
- 6 patients – stable disease
- 1 patient – complete remission (liver and primary)
- Sx from primary improved after initiation of chemotherapy
 - 1 patient required diverting colostomy for obstruction

“Liver First Approach” for patients with locally advanced Stage IV rectal cancer

Verhoef, Diseases of the Colon and Rectum 2009;52:23-30

- Median follow up 18 months (7-56)
- 16 patients completed treatment
 - 14 NED (7-56 months)
 - 2 alive with pulmonary mets (20 and 29 months)
- ~60% potentially curative treatment

	Both stages completed	Median follow up, months	Median OS, months	Recurrence rate, n (%)	3 yr OS (%)
Mentha, 2008	30/35 (86)	NR	44	20/30 (68)	60
Verhoef, 2009	16/23 (70)	18	19	2/16 (13)	89
Brouquet, 2010	27/41 (66)	25	50	19/27 (70)	79
DeJong, 2011	18/22 (73)	NR	36	6/18 (33)	41
TOTAL	91/121 (75)			47/91 (52)	

V Lam et al. A systematic review of a liver first approach in patients with colorectal cancer and synchronous colorectal liver metastasis. HPB 2014;16:101-108

Definitely unresectable



Liver – Definitely Unresectable – Palliative

Symptomatic*	Asymptomatic
<p>Need chemotherapy ASAP</p> <p>Surgery for primary:</p> <p>Minimize complications</p> <p>Promote fast recovery</p> <p>Colon</p> <p>R side – resection</p> <p>L side – more likely to divert</p> <p>Rectum – diversion only</p> <p>Palliative radiation if continued symptoms</p>	<p>Chemotherapy</p> <p>Surgery only if complications develop (10%)</p>

*If < 3 months life expectancy – avoid surgery

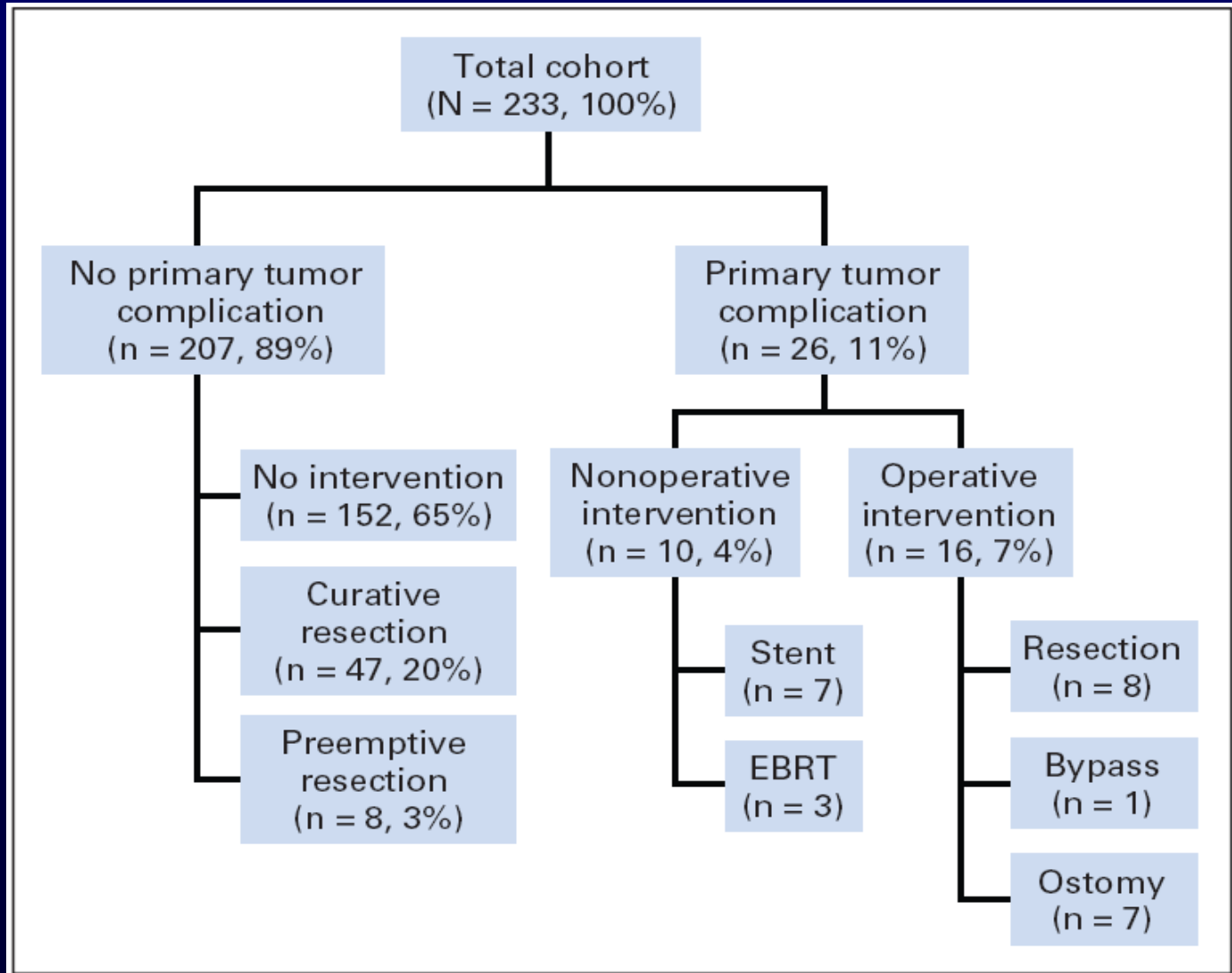
Outcome of primary tumour in patients receiving chemotherapy without surgery

Poultides GA. JCO 2009;27(20):3379-3384

- Retrospective study using prospectively maintained database
- 233 consecutive patients 200-2006
- Synchronous metastatic CRC with intact primary
- Received chemotherapy
- Complications of primary tumour
 - Surgery, radiotherapy and/or endoluminal stenting

<i>Median age, yrs</i>	60 (28-86)
<i>Primary tumour</i>	
Right colon	37% (87)
Left colon	29% (68)
Rectum	34% (78)
<i>Site of metastasis</i>	
Liver	95% (221)
Lung	30% (70)
Retroperitoneal nodes	39% (91)
<i>Number of sites of mets</i>	
1	40% (94)
2	45% (106)
3	12% (29)
4	2% (4)
<i>First Line Chemotherapy</i>	
FOLFOX	60% (139)
FOLFIRI	40% (94)
Avastin	48% (112)

Median overall survival – 18 months



Risk of emergent intervention not associated with age, location of primary, number of metastatic sites, avastin or CEA

Summary

- All patients with Stage IV disease need HPB assessment to assess “resectability”
- “Liver first” approach may be most useful in setting of borderline resectability of liver mets
- First line chemotherapy for unresectable CRC mets AND asymptomatic primary is effective and safe
- No high quality evidence to guide treatment
- Need to individualize treatment based on:
 - Tumour and patient factors
 - Patient preference
 - MCC