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

Liver - Definitely Resectable – Curative Intent

Symptomatic	Asymptomatic
Traditional approach	Traditional approach (Liver first approach)
CONSIDERATIONS: •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
Need chemotherapy ASAP Surgery to: •minimize complications •promote fast recovery *Colon* R side - resect L side – resect + divert *Rectum* Diversion only	Liver first approach (Traditional approach)

“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

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

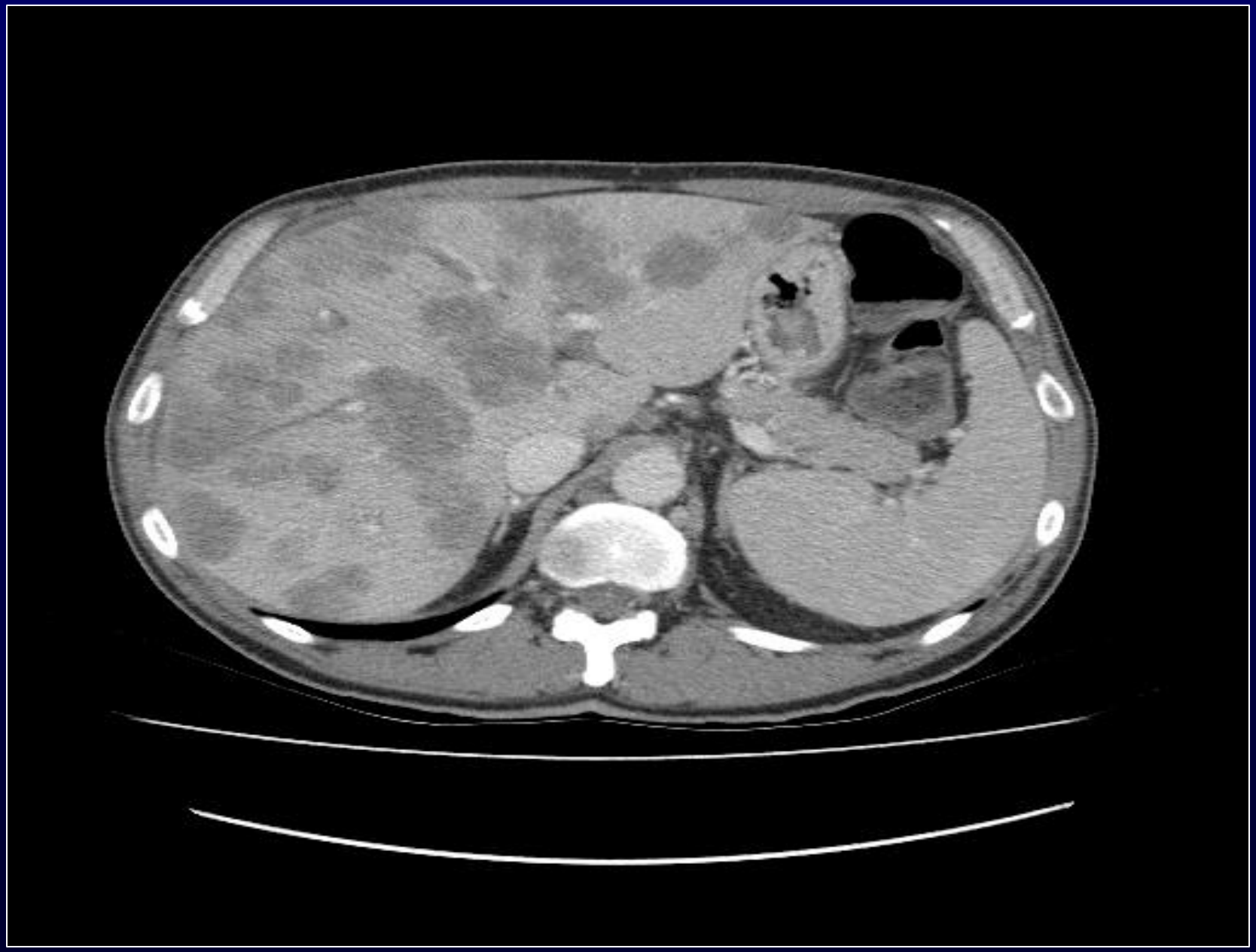
Verhoef, Diseases of the Colon and Rectum 2009;52:23-30

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

*If < 3 months life expectancy – avoid surgery

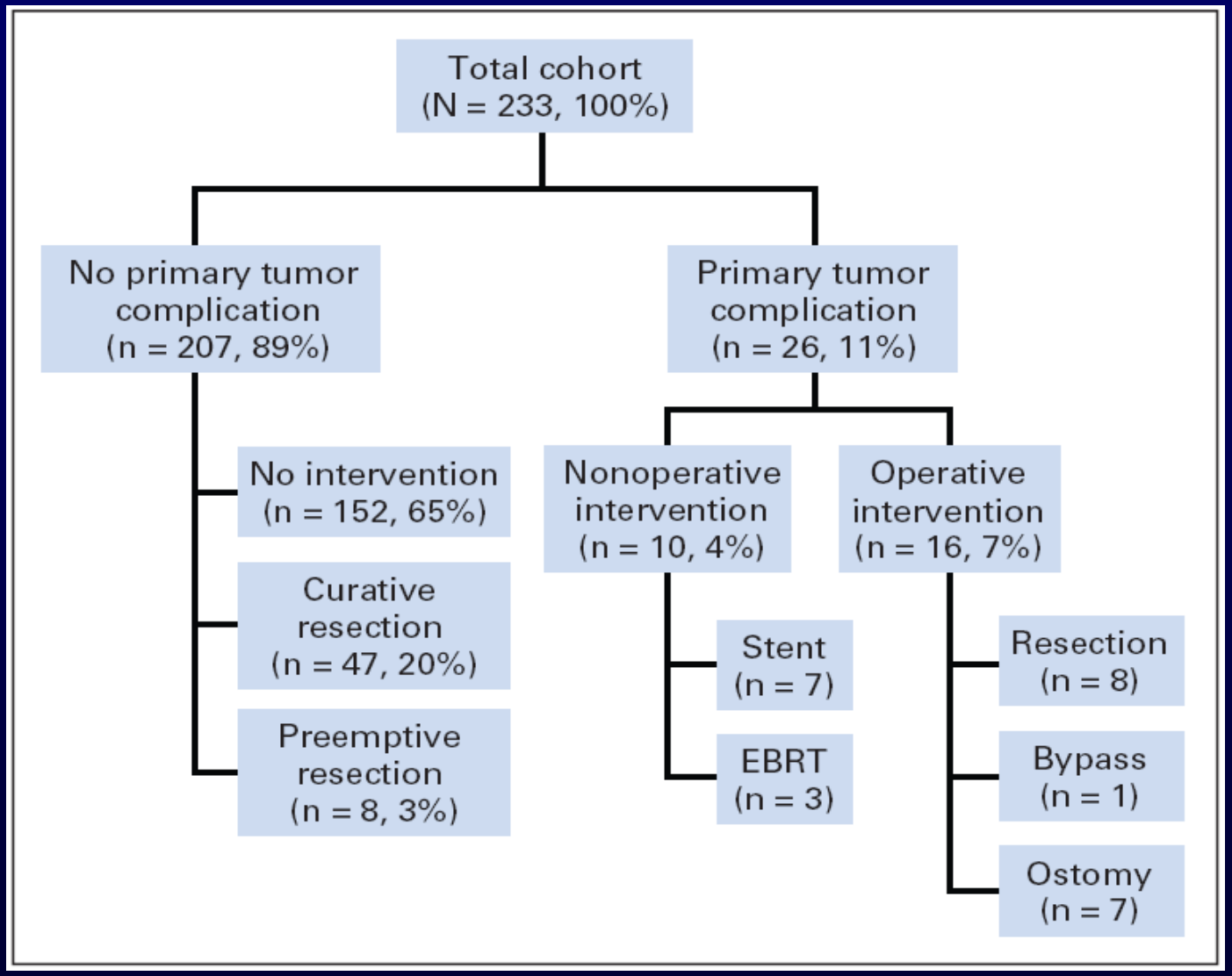
Outcome of primary tumour in patients receiving chemotherapy without surgery

Poultsides 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

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